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# Section of Neurology.

President—Dr. GORDON HOLMES, C.M.G.

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CASES SHOWN AT THE CLINICAL MEETING HELD AT THE NATIONAL HOSPITAL, QUEEN SQUARE, W.C.1, NOVEMBER 14.

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**Carbon Disulphide Intoxication.**—F. M. R. WALSHE, M.D.—P. P., aged 38, worked during 1926 and 1927 in an artificial silk works, attending to churns in which wood pulp was acted upon by carbon disulphide. Structural alterations in the churns were followed by a constant slight leak of their contents so that the workers were subjected to the carbon disulphide fumes. Patient's present illness began after about six months of this exposure. He first noticed a difficulty in concentrating attention on his work, and could not remember at what stage of the process he had arrived. He could not overcome a feeling of listlessness and indifference. At the same time he began to suffer from attacks of diarrhœa, nausea and vomiting, with abdominal pain and loss of weight. Several severe attacks of epistaxis also occurred at this time. The prominence of his eyes developed about three months after the initial symptoms; at first the left eye alone was affected, and this has always been more prominent than the right. Simultaneously his grasp became weak and his gait unsteady. At one time he could not hold a knife or fork with sufficient force to feed himself. He could only walk a few yards without resting and fell down on several occasions. Wasting of the hands and forearms became marked during the latter months of 1928.

All these symptoms were maximal in the spring of 1929, and since that time have steadily improved. He no longer complains of mental confusion, has no gastro-intestinal symptoms and is stronger and in better general health than at any time since onset.

Three fellow workers were similarly affected, but have not yet come under observation.

*Physical Examination.*—Alert and of normal intelligence. Visual acuity, $\frac{6}{6}$. Temporal halves of both optic discs somewhat pale, though probably within physiological limits. Pupils react normally; ocular movements normal in range and association; considerable proptosis of left eye and slight proptosis of right eye.

The sensory fifth is normal, but the masseters are rather weak. Pronounced bilateral weakness of face, especially of upper part, and left eyelids cannot be approximated over proptosed eye. Tongue normal; movements of deglutition and phonation, normal.

*Motor System.*—Slight general weakness of all upper limb movements, most pronounced distally. No ataxy. Muscles do not fibrillate and are not tender to pressure; slight wasting of the small hand-muscles. Power and coördination are normal in the legs, but there is slight hypertonus in the limb extensors.

*Sensory System.*—There appears to be a just appreciable blunting of cutaneous sensibility in all forms, over the extremities of all four limbs. Postural and vibration senses are normal

*Reflexes.*—Arm-jerks are of normal facility, knee- and ankle-jerks extremely brisk, but there is no clonus. Abdominal reflexes all present. Plantar responses, extensor. Gait normal.

Thoracic and abdominal viscera appear healthy. Blood Wassermann reaction negative; cerebrospinal fluid normal in all respects.

**Hepato-lenticular Degeneration.**—W. J. ADIE, M.D.—W. O., a girl, aged 11, has been unable to walk or to use her arms for a year.

*History.*—Born at full term; birth-weight 5½ lb.; no instruments used. Was slow in learning to walk and talk, and backward at school. At age of six the left foot turned in; about a year later the left arm went stiff; at the age of ten the right leg and then the right arm were similarly affected.

Always delicate but had no definite illnesses; was never jaundiced. Has a healthy sister, aged 14. No history of nervous disease or of liver disease in the family.

The prominent features of the case are: (1) Retarded mental development. (2) Fatuous expression and curious smile. (3) Extreme rigidity of the limbs with contractures. (4) Athetoid movements of right arm on voluntary movement. (5) Suggestion of defective liver function (lævulose tolerance test). (6) Absence of pyramidal signs.

**Pineal Syndrome (Ocular Palsies and Precocity) in a Boy of Twelve.**—W. J. ADIE, M.D.—A. C., a boy, aged 12, complains of headache, fits, double vision and shaking of the right arm, of one year's duration.

Nothing is known of his early history except that at the age of 8 he was "fully developed" and was not allowed to undress before his sisters.

His sexual development is that of a young adult. He is intelligent, but not precocious in book-learning. He is an incorrigible thief.

He presents, among others, the following signs: (1) Left pupil almost inactive to light; both pupils very sluggish on convergence. (2) Upward movements of eyeballs absent; downward movements poor; convergence very poor. (3) Coarse tremor of right arm of intention tremor type. (4) Internal hydrocephalus.

**Chronic Abscess of the Spinal Meninges.**—MACDONALD CRITCHLEY, M.D.—Female, age 18. Two and a half years ago had a septic arm requiring three operations. Four weeks afterwards had an attack of headache, backache, vomiting and fever, lasting about thirty-six hours. From this time similar attacks recurred, with great regularity, every nine days. Six months later was admitted to a general hospital where she remained under observation for over six months. Tentative diagnosis: rat-bite fever. The attacks gradually improved until Easter, 1929, when, after a particularly severe bout, the legs became weak. This was actually the last febrile attack, but weakness of the legs persisted and grew progressively worse. Gradually, numbness of the lower limbs, constant pain in the back and loss of sphincter control developed. On examination: spastic paraplegia with sensory loss, up to level of 6th thoracic segment. X-ray examination of spine revealed no abnormality; lipiodol was held up between the 5th and 6th dorsal bodies. Cerebrospinal fluid showed well-marked loculation syndrome.

*Operation*, August 2, 1929 (Sir Percy Sargent).—Mid-dorsal laminectomy; in the region of the 7th dorsal spine the dura was greatly thickened. When this was incised, a mass was discovered lying outside the cord, especially on its left lateral aspect. Portions of the mass and of the overlying dura were removed for investigation. Histological examination revealed that the mass was composed of highly vascularized granulation tissue containing numerous staphylococci. The portion of dura contained abundant infiltrations of plasma cells.

For the first three weeks after the operation there was a purulent discharge from the wound, which afterwards ceased altogether. There has been some return of movement and sensation to the legs and an obvious improvement in the general health.

**Progressive Ataxia in a Child with Positive Blood Wassermann Reaction.**—D. DENNY-BROWN, M.B.—G. B., male, aged 4 years and 2 months, admitted to hospital for unsteadiness in gait, which had been first noticed eighteen months ago, and had slowly and gradually progressed, and unsteadiness in the arms, which had been first noticed twelve months ago and had gradually progressed.

*History.*—Only child, parents married five and a half years ago. No other pregnancies. Labour not prolonged, forceps not used. Breast-fed. Perfectly healthy at birth and after, except for two attacks of "influenza," once two years ago, and once eighteen months ago (his mother also had influenza on each occasion). In each of these attacks he was irritable and feverish and vomited several times, but no other symptom was noticed. No convulsions. He was not late in learning to walk or to talk, and his gait was perfectly normal until the age of two and a half, when the unsteadiness was first noticed when he was chasing a dog on a garden lawn. He began to lisp slightly in speech about six months ago, but the lisp has not progressed. A month ago he said that his knees and toes ached, he was a little feverish (100° F.) and began to cough occasionally. The pains ceased the same afternoon and have not recurred. The cough continued up to the time of admission and he occasionally said that his throat felt sore.

No history of any similar complaint, or of deaths in infancy.

*Physical Examination.*—Bright, intelligent child, with head a little larger than normal. No stigmata of congenital syphilis. Colour good. Speech occasionally slightly lisping. Well behaved, clean in habits. Occasional dry cough with salivation. No defect in visual acuity and no field defect can be demonstrated. Slight pallor of both discs, maculæ normal. Pupils react briskly to light. Diplopia on looking to extreme right and slight deficiency in inward movement of left eye. Nystagmus on looking fully to either side, fine and rapid to right, slow and coarse to left. No defect in remaining cranial nerves.

No paralysis or paresis in any limb or trunk movement, but the limbs are all hypotonic and ataxic, with some coarse irregular action tremor in the upper limbs. No wasting. No involuntary movements. Tendon jerks all absent. Abdominal reflexes present and equal on both sides. Plantar reflexes both flexor. No sensory defect to pin prick, cotton wool, heat and cold could be demonstrated. Gait extremely ataxic and station very unsteady, with eyes open. Nasopharynx inflamed, no membrane. Culture from throat swab chiefly streptococci; no Klebs-Loeffler bacilli; marked reaction to Schick test.

*Cerebrospinal fluid* (October 22, 1929) clear, colourless, no cells seen. Total protein 0·025%; globulin tests, negative. Lange, no change in any tube. Wassermann reaction, negative.

*Blood:* Wassermann reaction, positive 3,300 (October 22, 1929), test repeated (October 29, 1929) with same result.

Skiagram shows skull of hydrocephalic type but with no other abnormality.

Blood Wassermann reaction of patient's mother is negative; his father is not in England.

**Jacksonian Epilepsy provoked by Stimulus to Right Foot or Right Ear.**—D. DENNY-BROWN, M.B.—A. P., female, aged 51, admitted to hospital on account of attacks of twitching of right side followed by unconsciousness. These attacks first began eight months ago.

No previous illnesses of any kind. Menstruation ceased at age of 48 years. Nothing pertinent in family history.

The first attack occurred in March, 1929. There was sudden unconsciousness without warning, lasting an hour, and followed by general weakness, misty vision and aphasia. Gradual recovery, complete in two weeks. Three weeks later she began to have attacks of unconsciousness preceded by twitching in the right hand,

giddiness, and a rhythmical clicking noise heard in the top of the head. These fits occurred once a day for a month and then she had treatment in bed for the following month and remained free from attacks.

At the end of May, 1929, she got up again and began to have attacks of unconsciousness whenever anything touched her right ear, or her head just behind the ear (for example, putting her spectacles on). These fits began with a twitching and tingling pain in the right side of the face and a clicking noise in the head. The twitching and tingling pain spread to the right hand and arm and then to the right side and leg. She remained conscious, but could not say what she wanted to say, during the attack. Weakness and numbness of the right side of the body lasted from one to twelve hours after each attack. The attacks continued on alternate days until July, 1929, when they began to occur each day and were followed by unconsciousness for 15 or 20 minutes; speech was limited to one or two words between the attacks and there was some continual weakness of the right arm. She was admitted to Cardiff Infirmary, and the only positive findings were weakness of grasp of the right hand and 10 cells per c.mm. in the cerebrospinal fluid. An exploration of the left parietal cortex was made (August 29, 1929). The arachnoid had a milky appearance round the superior cerebral veins, and the region of the "supra-angular gyrus" was "very soft"; "brain needles were passed in here but no fluid was obtained." The osteoplastic flap was replaced.

The attacks continued (one every two days), and six weeks ago the patient began to see, without warning, a blue light immediately in front of her eyes. This occurred at intervals of two or three days, and lasted twenty minutes each time. The light came and went rhythmically with the frequency of the pulse, and had no relationship to the time of occurrence of other phenomena.

Also six weeks ago she began to have attacks of unconsciousness, brought on by some particular stimulus to the right foot or the right leg below the knee (for example pulling a stocking over this foot). These attacks also began with clicking in the head and a tingling pain and twitching starting in the right foot and passing up the right leg and down the right arm to the face. They were followed by unconsciouness for a few minutes and by residual numbness, aphasia and increased weakness of right limbs for an hour or two.

For a month one or other kind of attack occurred every day, and she was afraid to touch her right ear and right foot. Once an attack was provoked no further attack was caused by touching either of these parts until about twenty-four hours had passed, and then some chance movement with contact at one or other part caused another attack.

During the last fortnight the attacks have been fewer, and she had not had one for a week previous to admission, in spite of frequent stimuli to the "sensitive" parts. Since August, 1929, she has had occasional double vision when looking to the right, and lasting an hour or so. She has frequently had difficulty in remembering the names of things and her husband's name during the last two months. She has not been able to write intelligibly since the beginning of August. She has often lately seen a large shadowy figure to her right side, but it is not there when she looks round and not there when she looks forward again.

*Physical Examination.*—Slight dysarthria of lingual type. Visual acuity $\frac{6}{12}$ right and left. No field defect to white or colours. Disc edges clear, colour good, vessels of normal appearance. Variable rapid nystagmus when looking to right, slow jerks when looking to left. Hypalgesia to pin-prick over right face. Other sensations unaffected. Corneal reflexes brisk and equal. Right palpebral fissure wider than left, weakness of right side of face. Palate moves slightly to left on articulation. Tongue protruded to right. Occasional very fine rapid tremor of left hand, but no weakness or change in tone, or incoördination in either upper limb or either lower limb. Tendon reflexes all present and equal on both sides. Left plantar response

flexor, right less definitely flexor, but not extensor. Abdominal reflexes absent on both sides.

Hypæsthesia to pin-prick and cotton wool over the whole right side. No inaccuracy to heat and cold. No astereognosis. Two-point discrimination equally accurate in both sides.

No bruit over any part of skull. Blood-pressure 115/70. Gait normal.

Cerebrospinal fluid: pressure 190 mm., 3 cells per c.mm. Total protein 0·065%; globulin tests negative; Lange, no change; Wassermann reaction, negative in cerebrospinal fluid and in blood.

Skiagram shows no calcification within skull.

Two attacks have been observed, each brought on by stimulus to right foot, one on October 26, 1929, and one on October 31; stimulation of right foot and right ear on each other day has not provoked an attack. First attack was produced by eliciting knee-jerk on right side; second by pulling bedclothes away from right leg. Both attacks began by tonic extension, followed by twitching, of right ankle, knee and then hip and then right arm, then right face and immediately following this, whole left side at once. Pupils inactive, no bruit heard over skull, no plantar responses (great toe tonically flexed). Duration of unconsciousness about four minutes, followed by aphasia and then marked perseveration, with weakness of right arm and leg and extensor plantar on right side, flexor on left. Complete recovery three hours after onset of attack, with return of all signs to those found on admission.

**Spinal Caries with Compression Paraplegia. (?) Syphilitic.**—HUGH G. GARLAND, M.R.C.P.—T. B., male, aged 62. Admitted to hospital, July 17, 1929, complaining of pain encircling the trunk at the level of the umbilicus, of eighteen months' duration. It is increased on coughing or sneezing. Six months ago weakness of the legs developed rapidly with incontinence of urine and fæces; three weeks later sphincter control returned and has been normal since. There has been numbness in both legs for two months with occasional flexor spasms. General health very good. Urethral discharge at age of 25 (untreated).

*Physical Examination.*—Some weakness of both legs with symmetrical muscular wasting and a mild degree of spasticity. Weakness of lower half of rectus abdominis. Hypalgesia over legs and lower trunk with impairment of temperature and vibration sensibility over same area. Upper border of sensory loss is at level of umbilicus, Gait slightly spastic. Knee-jerks exaggerated; bilateral knee- and ankle-clonus and extensor plantar responses.

Prominent veins over upper part of chest. Dullness to percussion at inner end of second left intercostal space and to right of eighth and ninth dorsal spines over an area about 4 in. in diameter with diminished air entry over same area. Marked prominence of eighth dorsal spine and of ninth rib on each side. Second aortic sound accentuated. Blood-pressure, 174/108 mm.

*Special Examinations.*—X-rays: Ninth dorsal vertebra is evenly collapsed; intervertebral discs and vertebral bodies above and below are normal. An opacity roughly circular in outline (4 in. in diameter) extends to right of collapsed vertebra and shows central patchy calcification. Bulging of descending arch of aorta, and continuous with this below is convex shadow of descending aorta (? displaced, ? dilated). Old fracture of eighth and ninth left ribs.

Cerebrospinal fluid: Pressure 100 mm., with no rise on jugular compression; slightly yellow fluid; 2 cells per c.mm.; protein 0·18%; Lange curve, negative; Wassermann reaction, negative.

Blood: Wassermann reaction 4444. Sedimentation rate normal.

Tuberculin skin test: Negative.

After a course of novarsenobillon, mercury, bismuth, and potassium iodide, the blood Wassermann reaction, the general condition, and the cerebrospinal fluid are unchanged.

**Pituitary Tumour, with Goitre and Acromegaly.**—REDVERS IRONSIDE, M.B.—J. B., female aged 60. Twenty-five years ago began to take larger shoes and gloves and noticed swelling appearing in neck. Fifteen years ago, retrosternal goitre partially removed on account of breathlessness, with residual paralysis of left recurrent laryngeal nerve. Patient complained of headache—never severe—during the past year. No giddiness, faints, or vomiting.

*On Examination.*—Typical acromegalic appearance, with hypertrophic changes in the interphalangeal and elbow-joints. Hard swelling in the region of the thyroid. Fields of vision bi-temporally constricted to red and green, but not to white. Skiagram of sella turcica shows considerable enlargement. Shotty glands in both supraclavicular regions. Symmetrical enlargement of submaxillary glands. Hæmorrhages in both fundi. Blood-pressure, 220/165. Urine contained a trace of albumin but no sugar.

**Polyneuritis Cranialis, Recovering.**—REDVERS IRONSIDE, M.B.—W. R., aged 18, a car-boy. Admitted to Guy's Hospital, under Dr. Poulton, August 8, 1929, on account of gradually oncoming right ptosis, noticed a fortnight before. Patient had felt in his usual health and his pulse and temperature had been normal. Within the past week he had noticed numbness over the right eye.

*On Examination.*—A pale, spare youth, with complete right ptosis. Optic discs, visual acuity and fields of vision, normal. Right pupil larger than left, reacting very sluggishly to light and on convergence. Left pupil normal. Complete external ophthalmoplegia, except for some power remaining in left external rectus. Sensory loss to pin-prick and cotton wool over first division of right fifth. Complete weakness of right face, upper and lower. Other cranial nerves normal. No deafness or otorrhœa. No sensory, motor or reflex abnormality. Urine normal. No glands palpable in neck. Spleen not enlarged.

Cerebrospinal fluid: 8 cells per c.mm.; albumin, 0·04 per cent.; globulin positive; Wassermann reaction, negative. Blood: pressure, 110 mm., Wassermann reaction, negative. This patient has never suffered from headaches or vomiting. Gradual recovery has been taking place. The pupils are now equal, central and circular, reacting to light directly and consensually and on convergence. Slight weakness of both external recti remains and there is slight right ptosis. Hyperæsthesia to cotton wool and pin-prick over the first division of the right fifth. Corneals brisk and equal. Slight right peripheral facial weakness. Other cranial nerves normal. No sensory, motor, or reflex abnormalities in trunk or limbs.

**Lesion of Third, Fourth, Fifth and Sixth (left) Cranial Nerves.**—LEWIS R. YEALLAND, M.D.—W. C., female, aged 27, in October, 1928, began to see double in artificial light. In February, 1929, diplopia became more or less constant and left eyelid began to fall. In July ptosis became complete and in addition she complained of stiffness and neuralgic pains in left face and loss of senses of taste and smell on left side. These symptoms have been gradually progressive except in January and June when there was, on both occasions, definite improvement for about a fortnight.

*Physical examination.*—Optic discs and fields normal. Left eye presents ptosis, internal and external ophthalmoplegia and proptosis. When the eyes are at rest a small portion of sclera is visible between the left eye and its external canthus. On attempted conjugate deviation to the right, the left shows inhibition. Inability to deviate jaw to right; wasting of left temporal muscle and weakness of left masseter. Left corneal reflex, absent; loss of sensation to pin-prick and heat and cold over all

divisions of left trigeminal nerve. A sensation of " small burn " is evoked on some contacts by pin-prick stimulus but not by thermal stimuli. Sense of taste lost throughout left side of tongue. The sensation of smell appears to be normal, although the patient is conscious of some defect. Examination of other cranial nerves showed no defect. Reflexes : right plantar is indefinite, otherwise reflexes are normal. The blood, cerebrospinal fluid, blood-sugar and skiagram of skull showed nothing pathological.

**Hæmatomyelia associated with Hæmophilia.**—H. J. SEDDON, F.R.C.S. (introduced by Dr. E. A. CARMICHAEL).—S. L., male, aged 24, chauffeur.

*History of Present Condition.*—June 9, 1928 : The patient was involved in a motor-car accident and admitted to Kingston Hospital. He was unconscious for three days as the result of " concussion." X-ray examination of the spine showed a fracture in the region of the third and fourth lumbar vertebræ ; there was some injury to the right ankle, but apparently no bony lesion.

He remained on his back for four months, and returned to work six months after the accident—not wearing any form of spinal support. After the accident he noticed that he occasionally lost control of his legs and fell. There was no paralysis and no loss of consciousness.

Early in 1929, he stumbled and injured his right hip. A large swelling appeared in the upper and outer part of the thigh but a skiagram did not show any fracture of the femur and the swelling gradually disappeared.

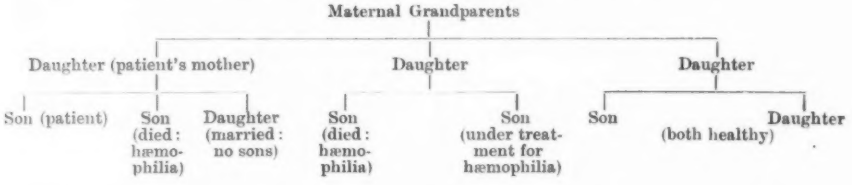
In May, 1929, right ankle " gave way " and the patient was admitted to hospital with a large swelling of that ankle, but, again, no fracture.

In June, 1929, after driving to Portsmouth—without accident—he became aware of sudden weakness in the left lower limb. The onset was instantaneous (he was having tea at the time) and there was severe burning pain in the left loin, radiating down the left leg. This persisted for ten days. He can recall " twitching " sensations in the paralysed muscles at the time of onset. The paralysis has been substantially the same since.

September, 1929.—" Pins and needles " were sometimes felt in the right lower limb, but there was no muscular weakness.

Micturition is normal and the bowels are kept regular by medicine.

*Family History.*—The history of hæmophilia is summarized below :—




*Past History.*—In 1926 patient was admitted to hospital on account of severe hæmaturia and remained there for six months. There were no marked constitutional signs.

*On Examination.*—Cranial nerves normal. Muscular action : Left leg, quadriceps extensor muscles not working. No voluntary contraction detected in pectineus and adductor magnus. Adductor longus and tensor fasciæ femoris working well. No other muscular weakness found. Sensations : An area in the left lower limb corresponding fairly closely to the distribution of the anterior divisions of L 3 and 4 is insensitive to cotton wool, pin-prick and differences of temperature. Vibrations of tuning fork not felt on left patella, and only felt poorly at upper and lower ends of fibula. General diminution in tactile sensibility in whole of left lower limb. Elsewhere no

sensory changes can be found. Joint sensibility is everywhere normal. Reflexes: Biceps, triceps, supinator and ankle-jerks strong and equal on both sides. Right knee-jerk easily obtained, left absent. Abdominal and cremasteric reflexes normal. Plantar reflexes flexor. Recent skiagrams show no abnormality of the spine. Lumbar puncture not performed, on account of blood condition. Urine normal.

**Dysarthria and Abnormal Gait: Case for Diagnosis.**—F. PARKES WEBER M.D., and O. B. BODE, M.D.—The patient, V. A., aged 25, is a strongly-built and well-developed man, who, when sitting at his ease, appears to be perfectly normal. His speech, however, is indistinct, and blurred or husky (not of the "scanning," disseminated sclerosis type), and when speaking he seems to be hampered by a spastic or hypertonic condition of the jaw-muscles. When he walks or when he stands upright (as if to attention) the upper part of his trunk is thrown rigidly back and slightly to the right, and, owing to very slight foot-drop, the left foot is raised somewhat more than the right. When he is speaking, the muscles of his neck and face tend to become spastic (see figs. 1 to 3). Besides the dysarthria he seems to have a little dysphagia.

FIG. 1.

FIG. 2.

FIG. 3.

Spasm of the right orbicularis muscle seems to have been a prominent feature, but disappeared nearly twelve months ago (see further on). There is very slight lateral nystagmus to left (not sustained). The tongue is always protruded somewhat to the right. The patellar and Achilles reflexes are over-active on both sides. There is ankle clonus on the left side, but not definitely on the right. The plantar reflex on the right side is of the normal flexor type, whereas on the left side it either cannot be obtained or a Babinski phenomenon is "indicated." There is no muscular incoördination. The maximum circumference of the left calf is 1 cm. less than that of the right calf; the circumference of the left thigh (20 cm. above the upper border of the patella) is 1½ cm. less than that of the right thigh. There is a slight difference at times between the two halves of the face, which may be due to slight muscular hypotonicity on the right side or hypertonicity on the left side.

Nothing abnormal has been noted in the arms, or in regard to the superficial abdominal reflexes, the pupils, the ophthalmoscopic appearances, or sensation anywhere. There are no tremors or abnormal choreic or rhythmical movements of any

kind. No muscular bradykinesia. No greenish coloration at the corneal margins. Nothing abnormal in regard to the liver, or spleen, or other abdominal or thoracic viscera, or in regard to the urine, excepting frequently slight excess of urobilinogen. The galactose test of hepatic function gives a negative result, and the blood-serum gives negative Wassermann and Meinicke reactions. The cerebrospinal fluid, when examined at another hospital, was normal and gave a negative Wassermann reaction. The patient seems to be of average intelligence, but perhaps almost abnormally cheerful (slight mental "euphoria"). Nothing abnormal in regard to emotional manifestations (crying, laughing, etc.) has been noted.

*Family History.*—The patient is said to have two healthy brothers, and in the family history there is nothing abnormal except that his father developed right-sided hemiplegia at the age of 28 years, and died of pneumonia at the age of 53 years.

*History.*—Operation for appendicitis as a boy. Articular rheumatism at 16 years. Suppurative middle-ear disease and mastoid operation five years ago. The patient has always been fond of muscular exercise, and can still stand on his hands with ease. In 1924 he had a job as labourer in London (using a sledge-hammer). When this job was over in 1925, he ran 32 miles in one day. On the following day he noticed that he was weak in the left foot, and that it tended to hang somewhat, and that in walking he had to raise it higher than the right foot; during the next two years he sometimes used a stick as a support. He thinks that the present illness commenced two and a half years ago with muscular spasms about the right eye, and what he calls "gasping" movements of the mouth. He has had neither the orbicularis muscle spasms nor the "gasping" movements for nearly twelve months. The peculiar gait, dysarthria and slight dysphagia have developed during the last seven months. There is no history to suggest that he has had encephalitis of any kind.

In regard to *diagnosis* one may think of some degenerative lesion affecting especially the motor tract to the left leg, together with a superadded functional disturbance; or (2) one may even think of the possibility of the whole syndrome being functional; or (3) an early and non-typical stage of chronic lenticular degeneration (Wilson's disease).

We have to thank Dr. W. R. Reynell and Dr. C. Worster-Drought for notes of the patient when in the West End Hospital for Nervous Diseases (August 15 to October 5, 1928), and Dr. M. Scholtz for the photographs which illustrate our account.

*Addendum.*—It seems that in his own home the patient sometimes walks normally, as for instance in crossing a room. He has done no work since 1925. At the meeting on November 14, a plantar reflex of flexor type was obtained, sometimes on the left side as well as always on the right side. The left ankle clonus was maintained even when the toes were forcibly flexed (Dr. Gordon Holmes). The tongue, after being protruded to the right, was likewise withdrawn on the right side (Dr. G. Riddoch). Not the least spasticity was observed when the patient voluntarily opened his mouth and protruded his tongue. The fact that a plantar reflex can often not be obtained on the side of the ankle-clonus is in itself very suggestive of a functional disturbance.

**A Case of Family Periodic Paralysis, with Attacks on Excitement.**—C. P. SYMONDS, M.D.—W. F., male, aged 28, locomotive fireman, has been subject to attacks of periodic paralysis since childhood. His younger brother, and his mother, are subject to similar attacks and the mother's father is said to have had the same complaint. The patient's attacks vary both in severity and duration; one, observed in hospital, lasted for an hour and a half and was of subacute onset. At its height all the voluntary muscles appeared to be affected, but none were completely paralysed. He was, however, quite helpless and inarticulate. All tendon-jerks were abolished. The plantar responses were flexor.

He states that although his attacks may come on without cause they are frequently occasioned by emotion. This may take the form of: (1) Excitement, e.g., the cinema, or an exciting moment in a game; (2) fear, e.g., when he receives a summons to go before his superior officer; (3) fluster, e.g., if when doing a job he realizes suddenly that he cannot get it finished in time.

The case is presented as affording a possible link between family periodic paralysis and cataplexy.

**Arterial Angeioma of Brain.**—C. P. SYMONDS, M.D.—G. G., male, aged 44, carpenter, first seen in March, 1929, on account of epileptic attacks dating from the age of 15. The aura consisted of a "wheel of shining blue and silver lights," revolving in a counter-clockwise direction in the right half of the visual fields. As a rule this was followed in one or two minutes by a generalized convulsion. Occasionally a brief vision of "people running about" intervened between the aura of coloured lights and the convulsion. He had been conscious since boyhood of a noise in his head, which he compared to the puffing of a distant railway engine. Recently he had complained of severe headaches and failing vision, and had had an attack of numbness down the whole left side of his body.

*On Examination.*—Showed marked dilatation of the outsides of the scalp especially over the left parieto-occipital area. A musical bruit, simultaneous with the carotid pulse, was audible over the whole head, being loudest above and behind the left ear. A skiagram showed grooving of the inner table of the skull by a greatly enlarged and tortuous vessel whose maximal girth corresponds to the left occipital pole. The visual fields showed an incomplete right hemianopia. Early papillœdema was present on both sides. There was bilateral exophthalmos. Both carotid arteries appeared large, and the heart was enlarged 1 in. to the left (confirmed by skiagram).

On April 2, 1929, Mr. Bromley ligatured the left common carotid artery, and the patient has subsequently been subjected to deep X-ray therapy. He has had no fits since the operation. Headache is less and papillœdema has subsided. The bruit, though still audible above and behind the left ear, is less evident both to physician and patient.

# Section of Anæsthetics.

President—Mr. R. E. APPERLY.

[*November* 1, 1929.]

## DISCUSSION ON AVERTIN ANÆSTHESIA.

**Dr. J. Blomfield :** During last Session we had two papers on preliminary medication in connection with anæsthesia ; the first dealt with most of the drugs used in this way, and spoke in detail of paraldehyde. The second was devoted entirely to paraldehyde, and some excuse might seem necessary for discussing another drug for preliminary use in connection with anæsthesia. Neither of the readers of those papers had, however, had any experience of avertin, and therefore Sir Francis Shipway and myself felt justified in bringing forward the subject of avertin anæsthesia, though avertin may be regarded as another instance of a drug which is useful as a preliminary to the administration of anæsthetics, rather than one which is itself an anæsthetic.

Avertin is tri-brom-ethyl-alcohol, and is a white crystalline substance which dissolves with difficulty in water to 3½%. When we began to use it we could only procure it in powder form, and the making of the solution was tedious, because it required prolonged shaking. But since then the makers have produced a solution, a fluid avertin, in which the avertin is held in solution by amylene hydrate. We now have a clear liquid, every cubic centimetre of which contains one gramme of avertin. This is added to distilled water heated to 40° C., and then the solution is ready for injection. The strength of the solution must be 2½% to 3%, and the dosage is determined by the body weight of the individual. We must have a rough guide when using anæsthetics of this kind, for we cannot feel our way as we go. We use 0·1 of a gramme per kilogramme of body weight of the individual ; this means using about two-thirds of a gramme per stone of body weight. The makers issue extensive tables in which the dosage is worked out in grammes and kilogrammes, and also in ounces and stones.

The technique of the injection is simple. The solution is run slowly into the rectum through a soft tube, inserted about 4 in. It is important that the anæsthetist should be present during the procedure because, as in the case of all anæsthetic drugs, people differ greatly in their reactions to avertin. If the anæsthetist is present he can safeguard the dosage, that is to say, he can measure approximately the susceptibility of the individual. Though the accepted dose for that person be 6 grammes in 200 c.c. of distilled water, it might be found when only 4 grammes had been used, that the patient was already unconscious and ready for the operating theatre. Fairly definite limits of dosage are stated, but even within those limits there may be unusual occurrences. Professor Eichholtz has said that even with the "safe" dose of 0·1 gramme per kilogramme of body weight, there may be dangerous symptoms in the case of weakly people ; but when the drug is used for persons of normal health, he has never seen or heard of dangerous symptoms being produced by the 0·1 gramme per kilo. Yet we have only to read the details of a case which, as it occurred in this country, probably came to the eyes of many of you, to find a contradiction to the professor's statement. The patient was a young man in ordinary health who was to have an operation for the radical cure of inguinal hernia. Anæsthesia, when he came to the theatre, was not sufficient for the performance of the operation ; it was supplemented by gas-and-oxygen only, and the patient left the theatre apparently in a normal state. Yet he never recovered, and died about eight hours afterwards. He had had a safe dose. The post-mortem

examination disclosed no cause of death. The case has not shaken my confidence at all. "To err is human." I think in that case there must have been some error undetected, and therefore unmentioned. In my own experience there has been nothing comparable to this. The young man had ½ gr. of morphine half an hour before the avertin, but he showed no sign of morphine poisoning, either during the operation or afterwards.

I early realized that avertin was a potent drug and must be used with care, because I had a case in which a very big and difficult patient received slightly more than 0·1 grm. per kilo. body weight: the dose was, in fact, 0·12. His condition on the table was excellent while a huge thyroid tumour was dissected out, but he never recovered, and died twelve hours afterwards. For some reason, that man did not eliminate his avertin. He too had had a sedative beforehand (omnopon gr. ⅓).

Generally, the induction of unconsciousness has been, in my experience, extraordinarily satisfactory; I think that to go to sleep by means of avertin is one of the pleasantest ways conceivable of becoming unconscious. I have not seen any excitement at all, and I have not had a patient who complained that there was anything unpleasant about it, except one young man, a nervous subject, who felt a strong desire to expel the tube from his rectum. Yet he was one of the most satisfactory in my series, because he had had several operations for removing exostoses, and for these he had had ether several times. He had always dreaded and hated the experience. He said that if in future he could have avertin he would not mind how many operations he had. The operation took between 30 and 40 minutes.

The induction is generally pleasant; there is no excitement or evidence of discomfort. The respiration generally becomes somewhat depressed, i.e., somewhat shallower and slower, a quieter respiration, not unlike that of sleep, except that there is some diminution in the amount of colour in the face, and stertor easily develops. The blood-pressure drops 10 to 15 mm.

The effect on the eyes is remarkable, because often, when the patient has been rendered unconscious by avertin, the corneal reflex is absent, and yet if a painful stimulus is applied, a reflex movement occurs, so there would be a movement at the first cut with the knife. I therefore do not rely on absence of the corneal reflex in avertin anæsthesia. To be sure whether or not more anæsthetic is required, the best test I have found is to place before the face a mask with a strong ether vapour for inhalation; if that is inhaled quietly without holding the breath, the operation can be begun.

Only about a fourth of my cases gave a satisfactory anæsthesia with avertin alone. Whether this happens or not depends on the nature of the individual and the character of the operation. The kind of case which has given me the greatest satisfaction has been that of a feeble, elderly individual, who had had gastrostomy for carcinoma of the œsophagus—the type of patient who may fail to recover after inhalation anæsthesia—exophthalmic goitre patients, and those who have taken other anæsthetics badly.

On the average there is from two to four hours' unconsciousness, but the coma is not of that deep variety which would make one afraid to use avertin in cases in which there may be blood about the air passages, nor is it coma as deep as after paraldehyde. I have used avertin for the dissection of tonsils without subsequent anxiety.

To sum up, my impression is that avertin is a very useful addition to our drugs, but that we should not attempt to use it as a routine in hospital. It is most valuable because it gives a very pleasant induction of anæsthesia, especially good for people who have had trouble with other anæsthetics, and it adds enormously to the safety of operations for exophthalmic goitre or on emaciated persons.

**Sir Francis Shipway:** The history of avertin, its chemical nature, its preparation and method of administration in man are by now so familiar, and its literature so extensive, that I do not propose to discuss them. My remarks are limited to a survey, from the clinical aspect, of the records of 106 administrations conducted at Guy's Hospital for a large variety of operations on patients with a wide range of age, many of whom were in a poor state of health, and to the impressions of the value of this new anæsthetic gained from a study of these records. I am indebted for the notes of six cases to Mr. C. H. Johnson, house-surgeon to the Throat and Nose Department, who was responsible for their administration; they include three cases of enucleation of tonsils in adults. In addition to obtaining the opinion formed by the patient of this method of induction and anæsthesia, I have obtained data of the length of the period of sleep and the occurrence of vomiting or nausea.

Solid avertin was used in the first forty-five cases, fluid avertin in the next thirty-three, in a 3% solution of distilled water. All the later patients have been given fluid avertin in a 2½% solution, which is stated by the manufacturers to give up the drug more evenly than the 3% solution, so that absorption is more gradual, and excitement and struggling are less likely to arise. This may be the case, although no example of excitement has been seen in patients for whom the stronger solution has been used. A real disadvantage, although perhaps a minor one, of the 2½% solution is the increased quantity of fluid which has to be injected; certainly the 3% solution appears to be preferable for children (who more readily retain small injections). The ordinary routine preparation by an enema on the night before operation, if this is to take place next morning, or in the early morning if operation is arranged for the afternoon, has been followed in all cases. The great majority of patients have been operated on in the afternoon. A rectal wash-out shortly before injection of avertin is to be avoided, as some of the liquid may remain in the bowel and interfere with absorption of the drug.

Of the 106 patients sixty-six have been males, with ages ranging from 12 to 72 years, and forty have been females, with ages ranging from 15 to 66 years; three were boys of 15 and under, four were girls of 16 and under, seventeen were over 55 years of age. In every case, except that of a boy to whom atropine gr. $\frac{1}{150}$ was given, morphine gr. $\frac{1}{8}$ to $\frac{1}{6}$ and atropine gr. $\frac{1}{100}$, or morphine gr. $\frac{1}{6}$, scopolamine gr. $\frac{1}{150}$ to gr. $\frac{1}{100}$, has been injected one hour before operation. The majority have received morphine gr. $\frac{1}{6}$, scopolamine gr. $\frac{1}{150}$.

The estimation of the correct dose is extremely difficult if full narcosis, or even the minimum amount of additional anæsthetic, is aimed at; body weight is an unscientific, and therefore uncertain, guide, because habits, occupation and temperament should be taken into account, and they are incalculable. The most that can be said is that certain types, e.g., the alcoholic, the active, the highly strung, react less easily to anæsthetics than do the abstemious, the sedentary, the placid. In the latter, smaller doses of avertin often produce adequate anæsthesia, e.g., a woman, aged 29, of calm temperament and indoor occupation was fully anæsthetized for an appendicectomy under a dose of 0·13, whilst 0·1 gr. was adequate for an operation upon the knee of a contented blacksmith who could neither read nor write. In the former types maximum doses will be necessary, and the risk of overdose will be run. For these reasons it is better to follow the doses now recommended and to be content with the result obtained, to aim, that is, at a safe, quiet, pleasant induction and to look upon avertin solely as a basal anæsthetic.

The doses that I have used have varied from 0·08 g. to 0·15 g. per kilo. (four cases); a dose of 0·12 g. to 0·13 g. has been used in forty-seven cases. The maximum quantity of avertin given has been 11 g. (dose of 0·125 g. per kilo.); five ounces of ether were used in addition; the operation was for inguinal hernia. In another case 10·5 g. were injected (0·13 g. per kilo.).

In no case has the condition before, or during, operation given cause for the slightest anxiety, in fact so satisfactory has it been that it was my intention to continue to give 0·12 g. to 0·13 g. to healthy adults of ages from 20 to 45 preceded by morphine gr. $\frac{1}{6}$, scopolamine gr. $\frac{1}{150}$. Following, however, the publication in the *Lancet* (March, 1929) by Dr. Blomfield and myself of the report of the Joint Anæsthetics Committee, Dr. H. H. Dale received a letter from Professor Eichholtz criticizing the use of doses higher than 0·08 g. for weakly patients and 0·1 g. for patients who are not weakly, on the ground that whilst some administrators had had very good results with the highest doses in many hundreds of cases, fatalities had undoubtedly occurred with 0·125 g. in patients who were not weakly and with 0·1 g. in weakly patients. The smaller doses recommended had been free from reproach and practically free from failure. Acting upon the strong recommendation of Professor Eichholtz, in my latest cases 0·08 g. to 0·1 gm. has been given, with, so far, very satisfactory results. These are the doses, then, that should be used, with the caution that old people need relatively less avertin. Professor Eichholtz further emphasizes the importance of noting the rapidity of the onset of sleep or rapid deepening of sleep; to prevent too deep narcosis, he says, the remainder of the injection should be at once let out of the bowel. This precaution can only be adopted in clinics where the injection is either given by the same person who can make herself familiar with the phenomena of what may be termed a normal induction, or supervised by an anæsthetist who is fully acquainted with the varying reactions of patients to anæsthetics.

Avertin has been used in this series for gastrostomy, gastro-jejunostomy, appendicectomy and other abdominal operations (seventeen) for removal of simple and malignant tumours of the breast, for operations on limbs, neck, nose, throat, and other parts of the body. In twenty cases avertin has been used alone; these include in addition to the two mentioned above, subjects suffering from hernia, hæmorrhoids, anal fistula in a man with active pulmonary tuberculosis, and carcinoma of both breasts (in a man aged 42). One case is of special interest as the patient, a man aged 29, weighing 12 st. 3 lb., was adequately anæsthetized by a dose of 0·1 gr. for enucleation of the tonsils, although the cough reflex was evoked by the application of a mask wetted with ether. In thirty-one cases gas and oxygen has been used in addition; this combination seems to be ideal. In ten cases ether was added to the gas-and-oxygen; a mixture of chloroform and ether in three cases; chloroform was given in one case for removal of a growth of the tongue by diathermy. In all the other cases (forty-one) ether has been used in amounts varying from 3 dr. to 7 oz.

Induction is quiet, smooth, and usually rapid, consciousness often being lost in the middle of a sentence a few minutes from the beginning of the injection. The whole process is entirely free from discomfort and takes ten minutes. The injection is given half an hour before operation. Anæsthesia deepens to its maximum in thirty minutes. The patient is kept lying upon his side to prevent obstruction to breathing; should the tongue be retracted during inspiration the head is well extended or an airway inserted. The colour is occasionally slightly cyanosed, as the respiration may be shallow and the rate decreased; the factors affecting the centre, viz., omnopon or morphine, scopolamine, avertin, amylene hydrate, produce different effects. Thus the centre may be stimulated or depressed, although the usual condition is one of depression, but in no case has any anxiety been felt nor has it been necessary to use a respiratory stimulant. Should the need arise, $CO_2$ would appear to be the most efficient of the remedies recommended. The pulse-rate is usually slightly increased. The blood-pressure falls about 15 mm. Hg; the maximum that I have observed was 30 mm. Hg. The pupil is small and reacts to light, the globes are fixed, the muscles of the lower jaw partly or completely relaxed, the conjunctival reflex absent, the corneal reflex usually just present. In ten cases this reflex has been absent. The patient is then ready for operation, and the problem arises whether anæsthesia

will be adequate. It is quickly realized that the ordinary signs of anæsthesia are but poor aids in solving this problem and that other tests must be used. Of these, the most valuable are the preparation of the operation-area with picric acid or iodine, and the application of towel clips; again, depression of the lower jaw will often elicit reflex movement.

Some patients have presented features of unusual interest. In one, fine rapid twitchings of the masseters occurred with rigidity of jaw and arms towards the end of a radical cure of inguinal hernia under avertin alone; a dose of 0·15 gr. had been given. Pulse-rate had fallen by 10, blood-pressure 30 mm. Hg. In four cases twitchings of the masseters and shivering were noted; the pulse-rate and blood-pressure had risen slightly. In two of these shivering was so marked that the rectal temperature was taken and was found to have fallen respectively to 98·8° F. and 97° F.; in the latter case the whole leg had been exposed during operation for extensive varicose veins. The patient was treated with an electric cradle on his return to bed and quickly recovered. No additional anæsthetic was given in two of these five cases. In two women with large ovarian cysts pressure of the tumour prevented the injection of the whole of the solution. Analyses of urine have been made by Dr. J. H. Ryffel in a few cases; the presence of albumin or blood has not been noted. One man, aged 27, developed bronchitis following operation for inguinal hernia; gas-and-oxygen was the supplementary anæsthetic. There was a history of a recent cold.

Irritation of the bowel has not occurred; the solution is always tested for hydrobromic acid immediately before injection. The importance of this essential precaution has been seen on three occasions when the solution was found to turn blue at once when tested with Congo red. The rectum is not washed out after operation.

The period of anæsthesia produced by the smaller doses (0·1 gr.) is about $1\frac{1}{2}$ hours. The patient having been put back to bed lying on the side or with the head turned to one side usually sleeps for some hours. The sleep is not deep, as the patient can be easily aroused and if necessary made to take fluid. He quickly sinks again into a sleep, from which he awakes refreshed some hours later without unpleasant memories and ready, in the vast majority of cases, to take nourishment. If scopolamine has been used the period of amnesia is often prolonged. All patients have expressed their delight with the method. Nausea and vomiting rarely occur, even after the administration of ether. One death which occurred some hours after operation calls for comment, although the notes of the post-operative period are scanty. The patient, a man aged 68, weighing 9 st. 12 lb., was admitted for severe gastric pain and loss of weight. He was of heavy build, bronchitic, and of alcoholic appearance, one eye was missing, on the other were corneal scars. A diagnosis of gastric ulcer was made. He was given morphine gr. $\frac{1}{6}$, scopolamine gr. $\frac{1}{150}$ and a dose of 0·12 g. (3 p.m.). At 3.45 he was well under, of good colour, respiration 20, pulse-rate 90, blood-pressure 115 mm. Hg. Incision was made at 3.47 p.m. and produced a slight reflex movement. C.E. was then given, and as the patient was resistant had to be pushed to such a degree both during exploration and again during closing of the abdomen that oxygen was necessary to relieve cyanosis. A posterior gastro-jejunostomy was performed. Operation lasted 62 minutes, and 3 ounces of C.E. were used; at the end pulse-rate was 120, condition fair. Pulse-rate had fallen to 64, but cyanosis was noted as being present. About one hour later the pulse-rate had risen to 98, the volume was poor, and cyanosis was still present. Oxygen and stimulants were then given, but the heart's action became progressively more feeble and the patient died at 9 p.m. Post-mortem revealed a very fatty heart muscle, and some cirrhosis of the liver. It will be seen that it is not easy to follow accurately the train of events and to estimate precisely the parts played by morphine, scopolamine and avertin; the patient was admittedly a difficult subject and a poor

risk for a major abdominal operation, but at least the opinion may be hazarded that early relief of cyanosis at the time when it was first noticed and the pulse was of good volume and rate (64), might have prevented the later development of cardiac failure. All other patients have made a good recovery.

Summing up my impressions of avertin which are admittedly derived from the observation of a small number of cases, I feel justified in saying that it is, if used with the care and in the doses recommended, a safe and valuable agent for induction, for providing an excellent basis of anæsthesia and for procuring a recovery which is remarkably free from after-effects. Its special indications are, I believe, for highly nervous and over-wrought subjects, and those who have suffered much from other anæsthetics, for patients with cardiac and pulmonary complications, for patients with exophthalmic goitre, and for some of those who have to undergo protracted operation, e.g., plastic. I do not include in the last class the patient who has to undergo an operation on the air-passages which requires the sitting posture during recovery, and I feel strongly that avertin is contra-indicated for operations which are likely to cause a rapid fall of blood-pressure, and for the subjects of severe renal disease.

**Dr. James Young** (Edinburgh) said that he had employed avertin in 154 unselected cases in his hospital and private gynæcological practice. This experience had led both his anæsthetist, Dr. James Robertson, and himself to regard it as possessing considerable value as a routine agent. It was superior to the ordinary methods in (1) the ease and comfort of the induction, (2) the freedom from post-operative vomiting, and (3) the freedom from the common post-operative respiratory complications. The absence of the straining incidental to post-operative sickness, rendered avertin especially valuable when the abdomen had to be opened or before plastic operations on the pelvic floor. In the case of operations on the pelvic floor, they advised withdrawing the solution from the lower bowel before the operation was begun. This was easily done by introducing a catheter after the legs were slung up on the lithotomy supports, and it obviated soiling of the operation area by the fluid which was apt to be forced from the bowel when the posterior retracting speculum was introduced into the vagina. The withdrawal of the solution did not interfere with the anæsthesia. Avertin was of special value in hospital work, because so much time between operations was saved by its use. In their experience, which was, of course, still limited, the recognized dangers of the anæsthesia had not obtruded themselves. The obstruction to the air passages by the relaxation of the jaw and tongue was easily overcome by the introduction of an artificial airway. In one case there had been considerable depression of the respiratory centre, which was at once removed by the use of carbon dioxide. These respiratory troubles had been fewer since they had restricted the pre-operative dose of morphine to one-eighth of grain. In several cases they had found a marked fall in blood-pressure, in one case by 50 points. Since diminishing the quantity of morphine, they had found it necessary to increase the inhalation anæsthesia.

In this series of 154 cases there had been two deaths (one after hysterectomy for acute prolapse in a case of submucous fibroid of the uterus, and the other in a long-standing case of pelvic infection). In neither case could the death be attributed to the avertin.

**Dr. I. N. Lewis** said he had used the anæsthetic in twenty-eight cases. He had noted that the patients on whom it had the most effect were those he would classify as "sub-thyroid"; those on whom it had the least effect were those who might be called "hyper-thyroid." This observation seemed to have some connection with the question of the elimination of avertin, and therefore it was decided to carry out an investigation. Possibly the stimulus to metabolism might have some effect in

increasing the rapidity of the excretion of the drug. There one might have a safety-valve by which the rate of recovery could be increased. The hyper-thyroid patients recovered more quickly than the others from the effects of avertin. In Germany a clinical investigation had been made on the thyroxin content and the time taken to recover. It was intended to investigate the point in animals.

In his own cases there had been no unpleasant incidents following the use of avertin. It seemed particularly useful in goitre cases.

**Mr. Frankis Evans** said that he had tried avertin in one case of exophthalmic goitre. The dose was 0·08 g. per kg. body weight. The patient was not asleep, but was muttering, and begged to be anæsthetized. He infiltrated her neck with novocain and adrenalin, and then gave gas-oxygen. When she came to the ward afterwards, she said that the operation had been performed while she was conscious, and that she had felt everything.

She had mistaken the local infiltration for the actual operation, and had regarded the gas-oxygen administration as an attempt to deceive her!

**Dr. H. E. G. Boyle** said that what struck him about the openers' contributions was the question as to the need for giving heavy doses of morphine, or morphine and scopolamine, beforehand. This, he considered, must place the patients in a somewhat dangerous position. He gathered from what had been said that avertin could be dangerous, and several deaths from its use had been mentioned. If avertin sent people to sleep so easily, why could not a smaller quantity be given than that mentioned by the two opening speakers, so that patients would be merely asleep, and the avertin be used, not as an anæsthetic, but as a form of pre-medication before the giving of an anæsthetic? He thought that this method would result in a more easy and safe anæsthesia than that produced by a heavy dose.

**Dr. F. P. de Caux** said that the great drawback to the use of avertin as an anæsthetic alone was the length of time it had to be given before operation. He had first tried to use it as an anæsthetic by itself, in twenty-five abdominal cases, and had been forced to use gas-and-oxygen or gas-oxygen-ether to render the anæsthesia at all satisfactory. Since then he had been using it instead of scopolamine and omnopon, for the nervous type of patient, in doses of from 50 to 80 milligrammes per kilo. of body weight. The more nervous the patient, the more avertin he used. He used it in preference to other drugs for bronchoscopy, in doses of from 100 to 130 milligrammes per kilo. of body weight, according to the type of patient with which he was dealing.

**Dr. C. F. Hadfield** said that a point worthy of notice about avertin was the excellent way in which it had been introduced into this country by the makers, through their own agents. When avertin was brought to notice here some years ago, an article upon it appeared in the *Observer* and to him (the speaker) it seemed to imply the annihilation of this Section, because it was said to be so wonderful that anæsthetists would no longer be required. Dr. Eichholtz, the inventor, later got into communication with Dr. H. Dale, and they realized that avertin was dangerous if used without proper control. In the interests of themselves and of the public, the manufacturers took a course which he (Dr. Hadfield) believed to be unusual, i.e., they abstained from putting it on the market in this country until it had been tested scientifically by a body of experts. They handed it over to the Anæsthetics Committee, of which both Dr. Blomfield and Sir Francis Shipway were members, and for many months they refused to issue avertin to anyone who was not authorized

to use it and who had not undertaken to report results to the Committee. This was the proper way in which to introduce new drugs into the country. It was not until the Committee's report appeared in the *Lancet* that the drug was placed on the market.

**Dr. Ramsey Phillips** said that little had been heard about the treatment of those cases which did not do very well. He had been present on one occasion when an alarming state of anoxæmia supervened on an avertin narcosis; one inhalation of carbon dioxide, given at his suggestion, had restored the patient immediately. In similar cases since then, carbon dioxide treatment had succeeded every time.

**Dr. Z. Mennell** said that he had no great experience of avertin, but for an ordinarily healthy patient he disliked rectal anæsthesia; the respiration was depressed, the breathing shallow, and often there was some cyanosis, which meant that the anæsthetist had to attend to the airway after avertin had been given, as in the case of any other anæsthetic. That raised an important point, namely, that the administration of avertin ought not to be left in the hands of nurses. When he and his colleagues had begun to use it, they gave too much omnopon or morphine; he considered that a large dose of either was unnecessary. Avertin anæsthesia did not suffice for surgical work; it reminded him strongly of the old hedonal anæsthesia. The corneal reflex was very sluggish, and in several cases had completely gone, but the patients responded to a brisk skin excitant. He did not think the corneal reflex was any guide in avertin anæsthesia, i.e., as to the depth of anæsthesia, any more than it used to be in hedonal or paraldehyde anæsthesia. The only advantage of avertin over paraldehyde was that the smell of the latter was absent; he had not realized that recovery from avertin was so much quicker. He did not think that sufficient relaxation for operation could be safely obtained with avertin as an anæsthetic *per se*, though as a preliminary narcotic it was useful. But, as Sir Francis Shipway had said, it was not yet known in what type of patient or class of disease it would be advantageous. Surely it would be a mistake to use it as a routine anæsthetic. A class of case for which it could not be useful was that in which there was bleeding, or was likely to be bleeding, in the air passages, as the prolonged sleep afterwards would be dangerous.

**Mr. Hope Carlton,** referring to Kendall's view of the unsaturated nature of thyroxin in Graves' disease and its pre-operative replacements by Lugol's solution, suggested that the post-operative crises which might occur after an operation for Graves' disease was due to the sudden liberation of unsaturated thyroxin, and that it might be expected that avertin anæsthesia would make these crises less common since the bromine in the avertin would, as a halogen, saturate the thyroxin. Other speakers had spoken well of avertin in operations for Graves' disease. Were these good results due simply to its action in allaying apprehension, or were they the results of iodine substitution on the lines he had indicated? One would not expect similar benefit in cases of toxic adenomata in which the thyroxin was already saturated.

**Mr. Geoffrey Keynes** said that he had not used avertin in many cases, but he hoped that by its help he might be able to eliminate ordinary ether anæsthesia in a number of operations, particularly abdominal ones. The first of his patients on whom avertin was used was one who required gastrectomy. The avertin was combined with a local infiltration of the abdominal wall and a splanchnic injection. That was completely successful. The patient only had 0·08 of a gramme per kilo. of body

weight; it seemed, indeed, to be an ideal form of anæsthesia. If that experience could be repeated he would propose to use avertin for most abdominal operations.

He was particularly interested in its use in operations for exophthalmic goitre for which he was in the habit of employing local anæsthetics only. Many of these patients, however, were very apprehensive, and it was a severe ordeal for them. He proposed in future to use avertin and local anæsthesia in combination for these cases.

He had been puzzled by Dr. Blomfield's remark that debilitated patients bore avertin badly, and then to hear him say that he included in his three categories of the cases most suitable for its use that of persons who had œsophageal obstruction and needed gastrostomy. He (the speaker) had long felt that for gastrostomy local anæsthesia alone was quite successful; nothing else was required. If it was dangerous for debilitated patients, he would imagine that avertin was not the anæsthetic to use in those cases. He had seen it stated that exophthalmic goitre patients were able to destroy the avertin more quickly than did other people; if that was the case, avertin anæsthesia was particularly safe for them and was the right anæsthetic to use.

**Dr. Blomfield** (in reply) said that when Mr. Keynes spoke of a combination of avertin and a local anæsthetic for abdominal operations he hit the nail on the head.

With regard to emaciated patients, he believed that in the case of feeble people requiring gastrostomy, avertin, given carefully and in small doses, was a good anæsthetic, and in his experience it was safe. Feeble people were easily knocked out by any anæsthetic, and so the dose should be reduced. In exophthalmic goitre cases also he thought Mr. Keynes would be satisfied with avertin, especially if he combined it with local anæsthesia. It was also true that such patients were safe subjects for avertin, presumably because of their excess of thyroxin; at present it seemed that the extra thyroxin added to the patient's safety, and that the subthyroid individuals were of the type for whom avertin was most dangerous. That was borne out by the fatal case of the large thyroid removal, there being very little thyroid tissue and thyroid secretion.

He had read that the combination of avertin with spinal anæsthesia was to be condemned; he did not know whether it was thought to be dangerous because of the lowering of the blood-pressure. He had not tried the combination.

He did not agree with Dr. Mennell's strictures with regard to blood in the air passages, and he did not think that the sleep induced by avertin was to be compared with that resulting from hedonal. Undoubtedly carbon dioxide was a valuable stimulus when a stimulus was required; he had not needed to apply any stimulus in these cases, but the first thing he would use if he had that need would be oxygen with 7% carbon dioxide. He agreed with Dr. Boyle's and Dr. de Caux's remarks; it was the correct principle in many cases to give only sufficient avertin for the perfect induction of sleep, and to rely on other agents for the true anæsthesia. But, as Dr. Mennell said, there was no one anæsthetic which was best for all cases and all classes of patients. As with other anæsthetics, it had to be used with discrimination; only in feeble people did avertin alone produce perfect anæsthesia.

Dr. Young had alluded to the use of morphine beforehand, and that was an important point. In most instances one could dispense with preliminary morphine or omnopon, but, if with an alcoholic or a resistant type of patient, some omnopon or morphine should be used beforehand.

**Sir Francis Shipway** (in reply) said that avertin was not dangerous if used with care and in selected cases, and was not contra-indicated for tonsil and nose operations, as the larynx remained sensitive during the post-operative sleep. He

had referred in his paper to the danger of giving avertin if a rapid fall of blood-pressure was likely to occur, e.g., during operation on the brain or following a spinal anæsthetic. To obtain relaxation in upper abdominal operations he used either ether, or a mixture of chloroform and ether. He preferred a combination of morphine gr. $\frac{1}{6}$ and scopolamine gr. $\frac{1}{150}$ or gr. $\frac{1}{100}$, to morphine gr. $\frac{1}{4}$ and atropine gr. $\frac{1}{100}$, as he had always found that the latter depressed respiration more than the former. He had not used avertin in the small doses suggested by Dr. Boyle.

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Sir FRANCIS SHIPWAY demonstrated the Guy's Hospital pattern of the Walton Gas-and-Oxygen Apparatus.

# Section for the Study of Disease in Children.

President—Mr. H. A. T. FAIRBANK, D.S.O., M.S.

[*October* 25, 1929.]

**Specimens from a Case of Malignant Goitre.**—ALAN MONCRIEFF, M.D. (for Dr. F. J. POYNTON).—The patient was a girl, aged 11 years, youngest of a family of six; no family history of goitre. Swelling of neck was first noticed at the age of 4 years. She had lived in Scotland most of her life except for a trip to

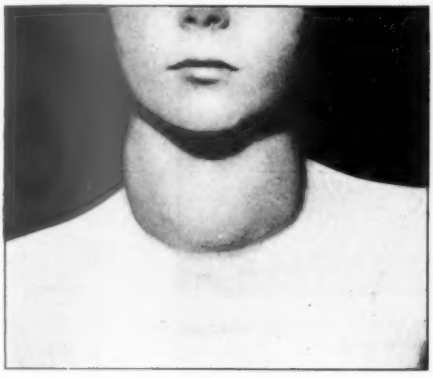


FIG. 1.

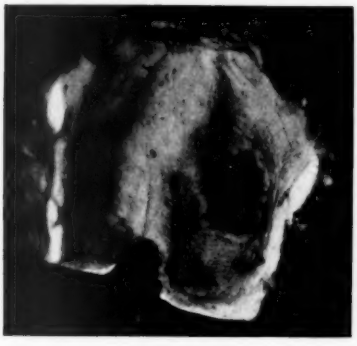


FIG. 2.

FIG. 1.—Case of malignant goitre (Dr. F. J. Poynton and Dr. Alan Moncrieff).
FIG. 2.—Trachea opened from the front to show growth infiltrating through on left side

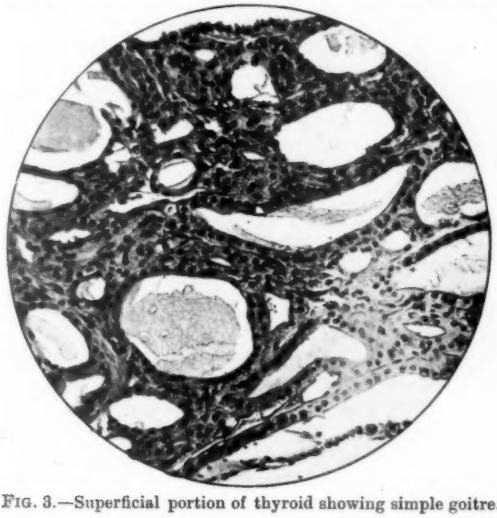


FIG. 3.—Superficial portion of thyroid showing simple goitre.

Australia. Various forms of treatment for the gland had been tried. For the few months previous to her admission to hospital there had been increasing noisiness in respiration and the gland had become larger. Adenomatous goitre was diagnosed

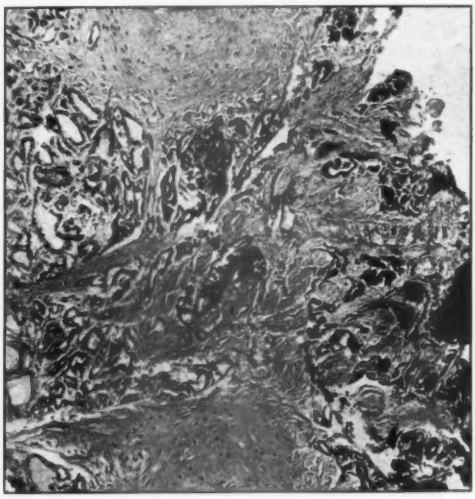


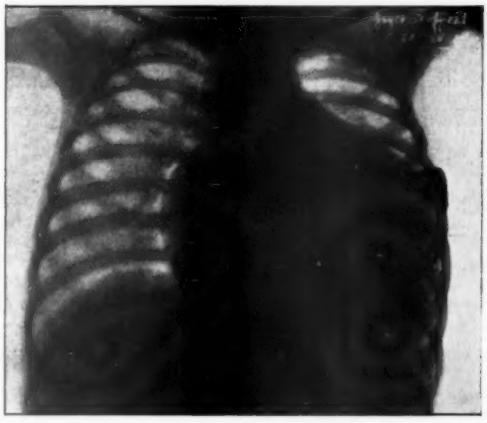
FIG. 4.—Deeper layers of thyroid, showing infiltration between two rings of tracheal cartilage.

and an operation was attempted to remove portions of the gland. This proved to be very difficult owing to unexpected adhesions, especially of the deeper portions of the gland, and the child succumbed twelve hours after operation. Only a limited examination of the operation area was permitted, but it was then found that the deeper portions of the gland were very hard and were adherent to the deeper structures of the neck; and, as shown in fig. 2, in one place the trachea was infiltrated with growth which protruded through, just below the larynx. Microscopical examination of the superficial portions of the gland shows a parenchymatous type of goitre (fig. 3), while in the deeper portions malignant change in the character of the cells is seen (fig. 4.)

Dr. F. J. POYNTON said that while this child had been under his care the striking feature was the rapidly increasing hardness of the tumour; when first seen it was not very hard. He had seen no way of avoiding an operation, though he had feared that it would be fatal, as the goitre was so large and the child was not strong.

**Three Specimens of Congenital Heart Disease.**—ALAN MONCRIEFF, M.D. —(1) *Idiopathic Hypertrophy of the Heart.*—Female infant, aged 1 year. Health stated to be normal until age of five months, when she had bronchitis. Following this, periodical attacks of difficulty in breathing developed; she was admitted into hospital during one of these, and the greatly enlarged state of her heart was then discovered. (See skiagram, p. 3.) No definite murmurs were heard. Blood-pressure 65 mm. Hg systolic; no sign of any secondary circulation. Urine normal. No cyanosis except during the attacks of dyspnœa, in one of which the child died.

The heart shows great dilatation of all the chambers, and especially of the left ventricle. No evidence could be found of any coarctation of the aorta at any situation. No sign of any congenital valvular or septal defect. On section, the heart-muscle stained well and showed no sign of any degeneration. There was a small infarct in the left kidney.



Idiopathic hypertrophy of heart.

(II) *Coarctation of the Aorta.*—Male infant, aged 3 months, who had been weak and ailing from birth, was brought to hospital in a desperate state and died within half an hour of admission, so that no physical examination was possible. It was observed that he was cyanosed; pulse, 160; respirations, 64.

The heart shows marked hypertrophy of the left ventricle with enormous increase in the thickness of the walls. At the site of entry of the ductus arteriosus into the aorta, there is definite narrowing and the aorta at this point is distinctly thickened.

(III) *Single Aorta and Patent Ventricular Septum.*—Female child, aged 3 years, mentally defective; cleft palate. Tonsils removed in hospital, August, 1929; slight cyanosis was then observed, and a systolic murmur was heard all over the base of the heart, without enlargement and without change in the second sound at the base. In September an attempt was made to repair the cleft palate, but the patient died under the anæsthetic. The post-mortem examination was made for the coroner by Dr. Thomas Rose, by whose courtesy I am able to show this specimen.

There is no abnormality in the auricles or in vessels entering them. The foramen ovale just admitted a fine probe. The ventricles are somewhat enlarged, and at the upper part of the ventricular septum there is an opening about 1 cm. in diameter. The aorta arises in a single tube from both ventricles, more from the left than from the right. The pulmonary arteries came off this main trunk on its left anterior aspect about 2·5 cm. above the valve segments, and the main arterial trunks about 1 cm. above this. Lying in front of the main trunk is a curious thin-walled vessel; its cardiac end appears to terminate blindly, and its distal end was, unfortunately, destroyed. Three cusps to aortic valve, apparently normal.

*Discussion.*—Dr. F. J. POYNTON said he wondered whether any Members had seen a specimen like the first shown by Dr. Moncrieff. The blood-pressure in this case, from which the specimen was taken, had been low, and there was no evidence of thickening of vessels. The condition seemed to be inexplicable.

Dr. MONCRIEFF (in reply) said that the term "hypertrophy" here was unfortunate, but he used it because that was the heading under which such cases had been grouped. "Idiopathic enlargement" would, perhaps, be a better term. The microscopical appearance of the portion of muscle which he had taken for examination from the more hypertrophied

portion was that of healthy muscle fibre. Comparing the second case with the first, one was struck by the tremendous hypertrophy of the wall of the ventricle in the case in which there was coarctation.

**Chondrodystrophia, followed by Normal Development.**—C. W. VINING, M.D.—M. M., female, aged 11 years, first seen at the age of 4½ years, on account of backward development. Did not begin to walk until 4 years old; although she could say single words at 18 months, speech at age of 4½ was still indistinct; her habits were clean from an early age. First teeth were cut normally, but most of them had fallen out before she was 3 years old. During the past few months the mother had noticed intermittent swelling of abdomen and face, always

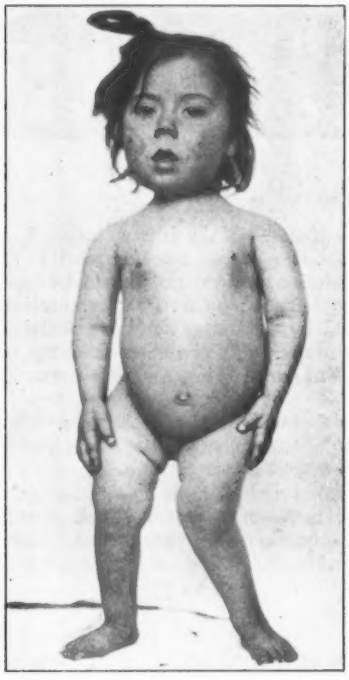


FIG. 1.—Chondrodystrophia. Condition at age of 4½ years. (Dr. C. W. Vining's case.)

more pronounced towards night; she says child's feet have never grown since she was a baby.

*Family History.*—Only four children alive out of ten pregnancies. Two miscarriages: four infants died before reaching the age of five years. One of these, a girl, who died from diphtheria, was said to have been just like the present patient. Of the girls, five had "bent legs," but only one of the three boys showed deformity.

*Condition at Age of 4½ Years.*—Height 32 in., weight 30 lb. At first sight she looked like a case of "fat" rickets. On closer inspection the shortening of the

upper arms and thighs was seen, but was thought to be due to rickety deformity; epiphysial enlargement at wrists was not obvious. Skull rather large, slightly brachycephalic, flat on the top with some bossing of the frontal and occipital regions. Fontanelle closed. Mental condition at this time was abnormal. This fact, together with the general appearance, suggested cretinism, but the mental condition, although subnormal, was not that of the cretin, the facial appearance was different, and the short upper arms and thighs were unlike the limbs of a cretin. Achondroplasia was considered, but the head, although rather large, was not typical of that condition. The face was different and the trident-shaped hands were absent. The feet were particularly small in size. X-ray examination showed a marked shortening, with thickening, of the humerus and femur, and their appearance, especially that of the humerus, suggested some osteoporosis. The skiagram of the wrist has unfortunately been lost, but so far as I can remember, it showed no gross rickets, and the lower end of the femur, while showing some indistinctness of the epiphysial line, is unlike that in a case of active and severe rickets.

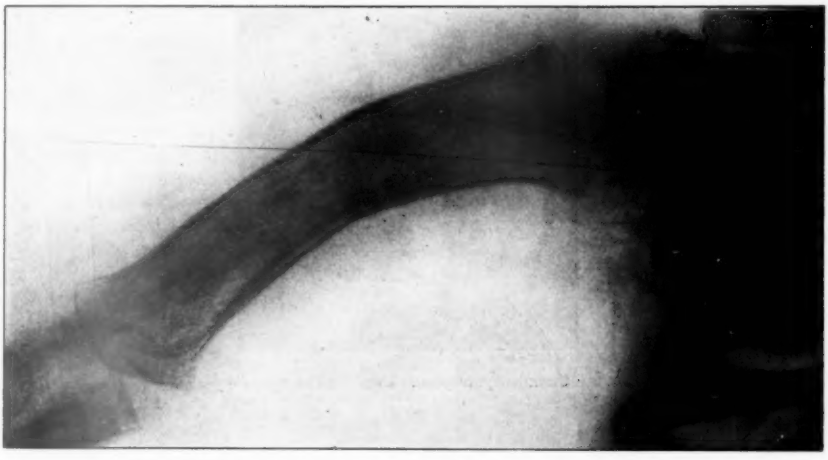


FIG. 2.—Chondrodystrophia. Skiagram of humerus at age of 4 years.

Wassermann reaction negative. Urine normal.

Treatment was begun with emulsion of cod-liver oil and one grain of thyroid extract daily. Improvement was rapid, and photographs taken at the ages of 6 years and 8 years respectively, demonstrate the return of the bones to a normal appearance and the gradual passing of the child from a grossly abnormal condition to one of normality. Apart from the brachycephalic type of head, the rather thick-set appearance, and some lordosis, her general appearance approaches that of a normal child of her age. Thyroid treatment was discontinued two years ago. Her mental condition, apart from some lack of ability to concentrate, is normal. She is attending an ordinary school. Her mother says she is extremely active, well behaved and good tempered.

TABLE SHOWING PROGRESSIVE HEIGHT AND WEIGHT

| Age (years) | Height (inches) | Weight (lb.) |
|---|---|---|
| 4½ | 32 | 30 |
| 6 | 36½ | 39 |
| 8 | 42 | 46 |
| 11 | 49* | 67 |

*4 inches below normal for this age.

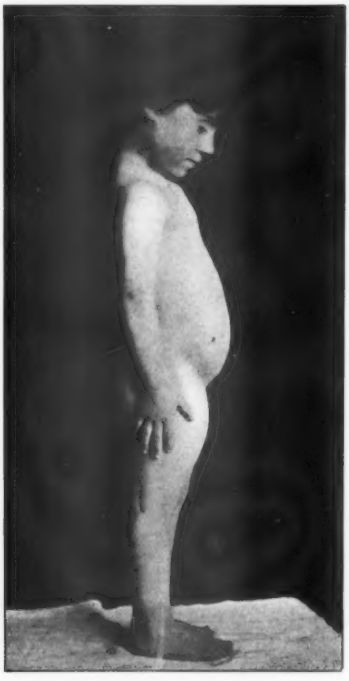


FIG. 3.—Chondrodystrophia. Condition at age of 8 years.

FIG. 4.—Chondrodystrophia. Skiagram of humerus at age of 8 years.

Mr. H. A. T. FAIRBANK (President) said that a few years ago he had tried to clear up, in his own mind, the complexity of the general bone diseases, but all he achieved was to realize anew the extraordinary difficulties of the subject, the chief of which was to classify the conditions indicated by the word "chondros," as it was difficult to know what a man meant when he used the various names. Dyschondroplasia meant a condition with a more or less unilateral distribution, the so-called "Ollier's disease," which was usually associated with short limbs. Some of these patients showed the mottled appearance, due to irregular ossification of the epiphyses, which was present in both the cases referred to to-day. He (the President) had had two cases in which the epiphyses had been so mottled as to suggest that the denser ossification areas had been flicked on with a brush; one met with all degrees up to the condition seen in the present case.

**Chronic Emaciation with Stunting of Growth.**—C. W. VINING, M.D.—P. P., girl, aged 2½ years, an only child, a full-time baby, weighed 8 lb. at birth. Fed with "humanized milk" up to age of six months, when she weighed 19 lb. Afterwards she was fed with a patent food. Progress uneventful except for persistent constipation, up to age of eleven months, when she began to lose weight and persistently refused to take any food except from a bottle. Insomnia was also a difficulty.

First seen at the age of eighteen months, weight 17 lb.; height 32 in. Extremely emaciated. Sixteen well-formed teeth present. Mental state precocious. Hair thick and curly. Abdomen not distended.

I took her into a nursing home, at which feeding was at once begun with a spoon. She took the food quite well, but refused to drink from a cup. At the end of a week the fluid shortage was becoming serious, so, much against my will, I reluctantly attempted to resume feeding by the bottle, but this was now refused. I then had the child removed to the infirmary, as a point had been reached at which either gavage or the giving of fluid by the bowel would be necessary. On reaching the infirmary she drank readily from a cup. She was in the infirmary for five months. She rarely slept, and was ready at any time, night or day, to be amused or to talk.

The stools never suggested cœliac disease. Two examinations were made.

| | First examination percentage | Second examination percentage |
|---|---|---|
| Total fat ... | ... 21·63 | ... 8·79 |
| Fatty acid as soap | 1·41 | ... 4·07 |
| Free fatty acid ... | 5·30 | ... 1·56 |
| Neutral fats | ... 14·92 | ... 3·16 |

Further, the child's appearance was unlike that in cœliac disease. She has always been free from physical signs. The carpal centres are normal. No thirst; urine not excessive in amount and normal in constituents. I have tried her with high fat, moderate fat and low fat diets, and we were satisfied while she was in the infirmary that she was taking sufficient food for her to put on weight, yet over a period of four months there, her weight increased by only four ounces. I have also tried anterior pituitary gland and a combination of pituitary with thyroid and adrenal, and I have given all the vitamins in turn; she has also had glucose with insulin. Blood sugar has been normal. Never any rise of temperature.

*Present Condition.*—Aged two years and eleven months. Weight 18 lb. 10 oz.; height 2 ft. 10 in. (has therefore only grown 2 in. in nearly eighteen months, but has put on 1½ lb. weight). Still extremely precocious and active. Is now taking a malt preparation with pepsin and pancreatin.

There appears to be some defect in the digestive function or power of absorption from the bowel which is retarding the development. There are no signs of dyspepsia, and a tendency to constipation is easily controlled. Her appetite is poor; possibly there is a condition of achlorhydria, but I have given her hydrochloric acid without result. She is at present gaining about 2 oz. per fortnight on a mixed diet containing moderate amounts of milk.

Chronic emaciation with stunting of growth. P. P., aged 2½ years. (Dr. C. W. Vining's case.)

I examined her again yesterday afternoon, and was unable to find any physical signs of disease. Mentally she is certainly most precocious; while I was examining her, she suddenly said "Do you think it may be indigestion?" So possibly she is after all a problem in psychology and nothing else.

**Splenic Anæmia, treated by Splenectomy (previously shown March, 1926).**[1]—JOYCE MORGAN, L.R.C.P., M.R.C.S. (for Dr. DONALD PATERSON).—On November 9, 1927, another hæmatemesis occurred, and a pint of blood was vomited. The patient was kept in bed at home for two weeks. Allowed up on November 23, whereupon there was further and more alarming hæmatemesis. Re-admitted to hospital under Mr. Rock Carling. Small amounts of blood vomited for two days. Blood transfusion performed; saline and glucose given *per rectum*.

December 29, 1927, discharged to rest in bed at home.

January, 1928, and subsequently, attended as an out-patient, and has been seen regularly since. General condition now shows steady improvement. The child is at school and looks very well.

*Recent Blood-counts.*—February, 1928: Red cells 4,530,000, hæmoglobin 48%, colour-index 0·53. White cells 6,800 (*Differential*: Polymorphonuclears 56% (neutrophils), monocytes 6%, lymphocytes 38%). Fragility: complete hæmolysis in 0·2% saline solution.

July, 1928: Red cells 4,100,000, hæmoglobin 60%, colour-index 0·7. White cells 7,500 (*Differential*: Polymorphonuclears 57% (neutrophils), monocytes 3%, lymphocytes 40%).

January, 1929: Red cells 4,900,000, hæmoglobin 67%, colour-index 0·7. White cells 8,500 (*Differential*: Polymorphonuclears 43% (neutrophils 38%, eosinophils 5%), monocytes 6%, lymphocytes 48%, myelocytes 3%). Fragility: normal.

[1] See *Proc. Roy. Soc. Med.*, 1926, xix (Sect. Dis in Child), 55.

*Discussion.*—Dr. H. FERGUSON TURNEY said that as there had been hæmatemesis since the operation the case could not be regarded as entirely satisfactory. The improvement which had taken place might be only temporary. Would the child be liable to hæmorrhage in the future, although the spleen had been removed?

Dr. JOYCE MORGAN (in reply) said that there had been no cirrhosis of the liver. She could not give an opinion as to the ultimate prognosis. The child had greatly improved since the operation. The blood-count was better than it had ever been, and she was certainly living a normal life.

**Pink Disease.**—JEAN SMITH, M.D. (for Dr. ERIC PRITCHARD).—B. S., female, aged 11 months. First seen when 8 months old. History of spots on the body for five weeks, and of extreme flabbiness since age of 4 months. Her feet and hands had been cold, blue and clammy for several weeks, and excessive perspiration had also been noticed.

*On Examination.*—August 2, 1929. Exceedingly fretful, resenting any interference. Extensive furunculosis of skin of trunk, while hands, arms and feet were covered with a fine pink macular rash and were bluish-red, swollen, cold and clammy. Mild degree of photophobia present. The child, who was unable to sit up, preferred to lie face downwards across the pillow. A few days after admission a fine desquamation of the pinhole type commenced on the palms and soles, and continued for four weeks. The muscles of the limbs were extremely flabby, rhonchi could be heard all over the chest, and a double otorrhœa was present. All the tendon and abdominal reflexes were obtained and we were unable to satisfy ourselves that there was any anæsthesia of the extremities.

Skiagram of chest and long bones revealed no abnormality. Blood-calcium 7·32 mg. Blood-pressure: 110 systolic, 75 diastolic; white blood-cells, 14,600.

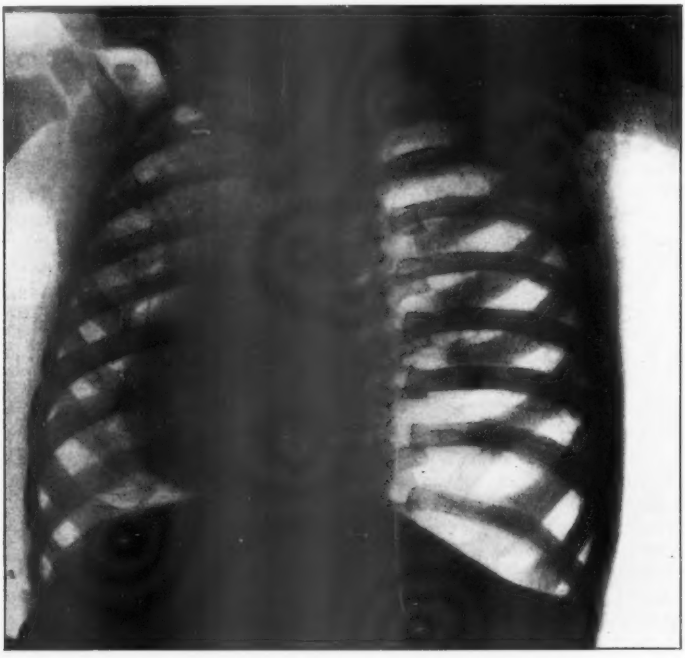
*Course.*—The child was gradually put on to a mixed diet with the provision of extra vitamins (A, B, C, D). On September, 16, 1929, a mild attack of measles developed, but did not seem to have any marked detrimental effect on the child, whose condition is slowly improving.

**Pink Disease.**—JEAN SMITH, M.D. (for Dr. W. E. ROBINSON).—K. W., female infant, aged 1 year and 5 months. The child was quite well until July, 1929, when she developed what appeared to be a cold. She became extremely irritable, screaming almost continuously. Eleven days later she became very drowsy during the daytime but restless and unable to sleep at night. Photophobia developed and she then assumed the characteristic position with the head buried in the pillow face downwards. At this time excessive perspiration and the eruption of a fine, pink, macular rash on the chest and abdomen were first seen. Some of the spots progressed to blisters. Anorexia has been a troublesome feature throughout. No falling out of the hair, nails or teeth has been noted. When seen at the Infants Hospital on September 19, 1929, the most marked features were irritability, photophobia, redness, swelling, coldness and desquamation of the hands and feet; excessive perspiration; anorexia; hypotonicity of all the muscles; sluggish knee-jerks and possibly some diminution in sensation to pin-prick on the hands and feet. The cerebrospinal fluid and urine were normal. A leucocytosis of 15,000 was present and the blood-pressure, although difficult to ascertain accurately, was about 120 systolic, 80 diastolic. There has been a slow, gradual improvement in her condition.

**Persistent Pneumothorax.**—HAZEL H. CHODAK GREGORY, M.D.—A male infant, aged 8 months, admitted to the Royal Free Hospital on account of pigeon-breasted deformity and persistent dyspnœa. Full-time baby, normal labour, birth weight, 9 lb., somewhat asphyxiated at birth; difficult breathing ever since; occasional bronchitis. On admission, child was seen to be well grown in height but under weight (12 lb. 14 oz.). He was pigeon-chested, with no asymmetry, breathed rapidly (40-50 per minute) and with exaggerated recession of lower thorax. Looked well, had a fair colour; no clubbing of fingers. Chest examination: Hyper-resonant

note over whole of left side, and breath sounds absent. Heart felt and heard to right of sternum.

Radiography revealed a complete pneumothorax on the left side with no sign of the left lung; a thin shadow as of some fibrous septum was seen traversing the cavity at about the level of the hilum. The right side was occupied by a lung with many patchy shadows, and the heart. It was then found that patient had been under Dr. Pearson at University College Hospital when three weeks old, when the condition had been diagnosed as "spontaneous pneumothorax." He had attended Great Ormond Street when 3 months old, and again the diagnosis was pneumothorax. He was taken home, but subsequently re-admitted with signs of acute bronchiolitis on the right side; he recovered after a week's severe illness.



Persistent pneumothorax, showing heart completely displaced to the right.
(Dr. H. Chodak Gregory's case.)

The chest was then investigated by X-rays. A needle connected with an artificial pneumothorax apparatus was passed into the left side. The fluid in the far limb of the water manometer shot up and overflowed, so that the pressure could not be measured at that time. (Subsequently a mercury manometer showed a positive pressure of 10 mm. Hg.) The bottles in the apparatus were reversed, and 500 c.c. of air withdrawn from the pleural cavity; the child then became faint and the withdrawal was stopped. A lung shadow was then seen a little to the left of the spine under the screen, but by the time a plate was taken, three minutes later, the shadow had disappeared, and the cavity was again full of air.

The persistent pneumothorax is obviously kept up by a bronchial fistula which was present at or soon after birth. There is no clue as to the causation of such a fistula; it may be congenital.

Is it possible to get that lung to expand by closing the fistula? The operation would not be so severe as it would in a child without a pneumothorax, and it would seem possible to explore for the fistula and then close it, thus giving the left lung a chance of expanding,

[Dr. E. U. WILLIAMS demonstrated the skiagrams on the screen. He said there was a report that dextrocardia was present at the age of 3 weeks, but he thought the condition had probably always been the same.]

*Discussion.*—Dr. B. SCHLESINGER said he had seen this case some months previously, and it had puzzled him. He agreed with Dr. Chodak Gregory that there was probably a bronchial fistula, but he would be chary about operative procedure, even in the able hands of Mr. Waugh, particularly as he did not think the lung would ever expand again.

Dr. A. G. PHEAR said the suggestion that there was congenital absence of the lung was a difficult one to support. On that view it was not easy to see why there should be pneumothorax at all. Assuming that there was a bronchial fistula, he thought something should be done to discover whether it was possible to close it. The condition of the child at the present time was precarious; there had recently been an attack of broncho-pneumonia, from which it had recovered; that piece of good fortune, however, was not likely to be repeated should there be another attack.

Dr. CHODAK GREGORY (in reply) said she agreed that probably the child would not be able to recover from another attack of broncho-pneumonia; though he had gone through the last without signs of fluid on the left side. Before operation she intended to explore with lipiodol, though she had not much hope that it would reveal the site of the fistula.

**Coarctation of the Aorta.**—BERNARD SCHLESINGER, M.R.C.P.—M.T., aged 11 years. *History.*—Pulsation in neck first noticed at age of 1 year, when heart was known to be abnormal. Pains in limbs when 3 years old, and again when aged 7. These pains usually seem to follow "colds."

*On Examination.*—Marked pulsation of carotid arteries and in suprasternal notch. Collapsing pulse at wrist; subscapular arteries palpable and collapsing, but abdominal aorta, and femoral and dorsalis pedis arteries felt only with much difficulty.

Heart enlarged; cardiac impulse in the sixth and seventh interspace. Left border of cardiac dullness in mid-axillary line; no enlargement to right; upper border in second space. Systolic and diastolic murmurs in aortic area and immediately to left of sternum; systolic bruit at apex, also well heard over the back.

Dr. F. PARKES WEBER said this was an excellent case, and he would go further than Dr. Schlesinger and say that it not merely might—but must—be stenosis (coarctation) of the aortic isthmus, of the adult type. He did not, however, agree with the exhibitor's suggestion that the cardiac murmur might possibly be due to a patent ductus arteriosus, as that would quite negative the exhibitor's original diagnosis. As far as the speaker was aware, in no true case of stenosis of the aortic isthmus had a patent ductus arteriosus been discovered at necropsy; in fact, "coarctation" of the aortic isthmus might be regarded as an extreme degree of closure of the ductus arteriosus. It was a closing or stenosing of the aorta at the region of the entry of the ductus arteriosus, due to an excess of the "closing process." It was far more likely that the murmur was due to aortic incompetence. In this case, he suggested, there was a slight congenital valvular malformation at the aortic orifice, for instance, a bicuspid orifice, such as had several times been found in association with aortic isthmus stenosis. Owing to the extreme extra strain thrown on the heart, as the result of the isthmus stenosis, there were possibly also secondary changes at the aortic valves.

**Severe Rickets with Anæmia.**—T. PEARSE WILLIAMS, M.D.—I. M., female, aged 4 years and 9 months.

For twelve months before admission parents noticed that legs were becoming bowed and child was growing paler. Early in September, 1929, an attack of diarrhœa developed, lasting one week and followed by a severe epistaxis. The nose was packed, but the next morning when the packing was removed the bleeding began again. Admitted to Paddington Green Children's Hospital, September 3, 1929.

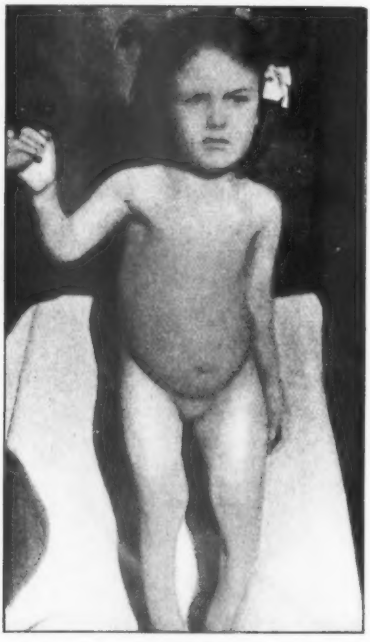
*On Admission.*—Marked pallor, collapse and air hunger; heart and lungs normal; teeth carious and dirty; tonsils enlarged and inflamed. Skeletal system showed the marked deformities now seen. Blood-system: Generalized purpura; liver and spleen not felt; no obvious enlargement of lymphatic glands.

*Blood-count*: Red cells 1,240,000, hæmoglobin 25%, colour-index 1·0, normoblasts 105, thrombocytes 2,500. White cells 7,000 (*Differential*: Polymorphonuclears 53·25%, lymphocytes 41·5%, mononuclears 4·75%, eosinophils 0·25%, basophils 0·25%).

Bleeding-time not increased. Wassermann reaction negative.

Slight poikilocytosis, punctate basophilia and polychromasia.

Early treatment: Hæmoplastin, nasal plugging. Later: Hepatex, radiostoleum, cod-liver oil and iron.



Severe rickets with anæmia. (Dr. Pearse Williams's case.)

October 10, 1929: On the suggestion of my house-physician, Dr. Rayner, patient was placed on irradiated milk.

There was irregular fever during the first month; urine normal.

*Blood-count* (Dr. H. W. Perkins, October 10).—Red cells 3,890,000, hæmoglobin 50%, colour-index 0·65, thrombocytes 155,000. White cells: 8,500 (*Differential*: Polymorphonuclears 68·8%, lymphocytes 26·0%, mononuclears 2·4%, eosinophils 2·4%, basophils 0·4%). Many poikilocytes. No nucleated red cells, slight polychromasia. Bleeding time not increased.

There is evidence, in such history as could be obtained, of neglect and unsound diet. For the first few days the child constantly demanded "beer and buppy."

Her health has greatly improved, and on the advice of my surgical colleague, Mr. C. W. G. Bryan, she is shortly to be transferred to a country hospital for treatment of the deformities. The skiagrams are informative.

# Clinical Section.

[*November* 8, 1929.]

**Neurofibroma of Cervical Region with Involvement of Hypoglossal Nerve.**—C. WORSTER-DROUGHT, M.D., and T. R. HILL, M.B.—A. W., male, aged 24. First complained in the spring of 1926 of weakness and some wasting of the left arm. About the same time he noticed a shrinkage of the left side of his tongue. Eight months ago a tumour appeared on the left side of the neck, which gradually increased in size.

*Family History.*—Father is said to have died from a "growth in the back," and a brother from a "growth in the neck."

*Physical Examination.*—When admitted to hospital in June, 1929, his condition was as follows: There was a large swelling on the left side of the neck, deep to the sterno-mastoid, and extending from behind the clavicle into the posterior triangle. It was hard and immovable.

The tongue, on protrusion, deviated to the left, and the left side was atrophied and showed a vermicular tremor. Other cranial nerves normal except for occasional twitching of left side of face.

Left tonsil much enlarged: Right middle-ear deafness.

Left arm showed some general wasting, circumferences of the upper arm and forearm being, respectively, 1 in. and ¾ in. less than those on the right side. No actual paresis but motor power is generally reduced, the muscles of the hand supplied by the ulnar nerve being especially weak. Reflexes: deep reflexes of left arm slightly reduced as compared with those of right arm.

The knee- and ankle-jerks are very sluggish but otherwise the lower limbs are normal.

*Sensation.*—Normal in left arm and elsewhere.

Pityriasis versicolor over anterior part of trunk, in axillary regions and extending on to arms.

Other systems normal.

*X-ray examination* showed a solid homogeneous mass, with sharply defined margins, lying in the left supraclavicular fossa, obscuring the apex of the lung, and extending down to the level of the first rib. It was pressing slightly on the left side of the trachea but caused no deviation.

*Blood.*—Wassermann reaction, negative. Blood-count normal.

On June 28, 1929, the mass was explored by Mr. Ramsay. A rounded tumour about 2½ in. in diameter was found protruding from beneath the centre border of the scalenus anticus muscle 2 in. above the subclavian artery. It was white and glistening and was freely movable in a lateral direction but not towards the spine or the left arm. It appeared to be connected with one of the cords of the brachial plexus and was continued as a finger-like process into one of the cervical intervertebral foramina. A portion only was removed as it was considered impossible to excise the entire tumour.

To the naked eye the tumour on section looked greyish-white and homogeneous. Microscopically, it consisted entirely of fibrous tissue, no nerve-fibres being seen (H. C. Lucey).

Apart from the diminution in size of the tumour (part having been removed) and the presence of the operation scar, the condition remains as described above.

*Commentary.*—The supraclavicular tumour appeared this year and has increased very rapidly in size. The clinical condition and the result of operation suggest either that the tumour arises from the hypoglossal nerve on or shortly after its emergence from the base of the skull and that it has gradually spread downwards

along the left side of the cervical spine partly to involve the cords of the brachial plexus; or that there are two separate tumours—the one palpable and partially removed at operation, and the second involving the hypoglossal nerve at a higher level.

In the absence of pigmented spots and evidence of further tumours, the term "neurofibromatosis" is probably more applicable to the case than "von Recklinghausen's disease."

**Chyluria.**—H. MORLEY FLETCHER, M.D.—V. R., female, aged 17, French polisher. Admitted to St. Bartholomew's Hospital April 12, 1929, on account of abnormal appearance of urine.

*Family History.*—Unimportant.

*Past History.*—Rubella at 2. Measles at 3. Scarlet fever at 10. Menstruation began at 14, quite regular until last few months, since then irregular. In 1926, box fell on foot causing an ulcer on dorsum, which took long to heal and still causes pain. Since September, 1928, has noticed that the urine was white, resembling milk, no unusual odour, no pain on micturition or increased frequency. General health good. No loss of weight. Has never been abroad.

*Present Condition.*—Healthy looking, good physique. Nervous, respiratory and cardiovascular systems normal.

*Abdomen.*—Dark-brown linear nævus on right side; no organ palpable; no tenderness; no palpable lymph glands.

*Pelvic Organs.*—Dr. Barris reported uterus normal in size; nothing abnormal detected in the appendages on either side.

*Rectal Examination.*—Nothing abnormal.

*Right Foot.*—Area of blue discoloration on dorsum, surrounded by areas of brown pigmentation; skin intact but thin and shiny; slight œdema in region of ankle and foot. No bony abnormality discovered on examination by (X-rays).

*Blood.*—Wassermann and Sigma tests negative. Blood cholesterol, 177 mgm. per 100 c.c.; blood-urea, 39 mgm. per 100 c.c.; blood-sugar. 133 mgm. per 100 c.c.

*Blood-count*: Red blood-cells 5,120,000, Hb. 80%, colour-index 0·8, white blood-cells 7,200.

*Urine.*—Milky appearance; specific gravity usually between 1020 and 1030; acid reaction; no casts; albumin occasionally present; no sugar; urea 2·4%.

*Cultures.* A few colonies of *Staphylococcus epidermidis albus.*

On the first examination it was thought that the milky character of the urine was due to the presence of a lipoid-globulin compound, and was a pseudo, not a true, chyluria.

Dr. Harrison found that under the microscope with ordinary lighting no fat globules were seen, but with dark ground illumination, myriads of minute fat droplets were visible. He reported as follows: No casts in the urine, and the amount of albumin varied in proportion to the amount of milkiness.

Occasionally the patient passed flocculent semi-gelatinous masses in the urine which consisted of fibrin, in which were entangled numbers of squamous epithelial cells, a few red cells and leucocytes, and triple phosphate crystals.

In order to establish further the fact that this was a case of true chyluria, Dr. Harrison devised the following experiment: 10 gm. of butter, containing 100 mgm. Sudan III, was given to the patient at supper on July 7, 1929, and the urine was collected at intervals up to thirty-five hours afterwards. The samples of urine showed no obvious pink tinge. Each was then extracted with ether, and the ether extract of the urine passed eleven and a half hours afterwards was obviously red, and that passed fourteen hours afterwards was pale pink, but the extracts of the other samples contained no dye.

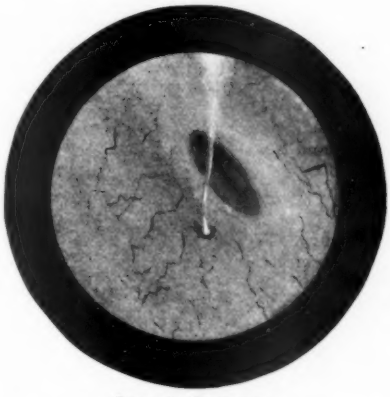
Two control observations after using the same quantity of dye were made on healthy males, and the urines yielded no dye to ether extraction up to thirteen hours.

This would show that, in the case of the patient, there was a direct leakage of chyle containing the pigmented fat into the urinary passages.

If the dye appears in the urine, a connection between the lymphatic system and the bladder is practically proved, as Sudan III is soluble in fats but insoluble in water, and normally most of the 100 mgm. is absorbed and deposited in the fat depôts and none appears in the urine.

June 1, 1929.—Mr. Girling Ball made a cystoscopic examination. Both ureters were catheterized; catheters passed full length quite easily. Urine drawn off from each ureter was quite clear and normal.

June 6, 1929.—Mr. Ball again made a cystoscopic examination. Urine from both ureteric orifices was normal and free from milkiness. A thin stream of thick creamy material was seen to be flowing freely from a minute orifice just on the trigone side of the right ureteric orifice, which was discharging a clear efflux. The opening was too small to admit a fine bougie.



CASE OF CHYLURIA.
Drawing of bladder showing left ureteral orifice and below it a minute sinus from which issues a milky stream.

October 25, 1929.—Mr. Ball made a third cystoscopic examination. Urine withdrawn from bladder was perfectly clear and normal in appearance. The orifice was quite clearly seen but was not discharging at the time.

Tuberculin skin reaction negative. Skiagram: No abnormal kidney shadows.

The cause of the chyluria was obscure; it seemed probable that it might be due to the presence of tuberculous glands, tuberculous peritonitis, or possibly an old inflammation of the appendix.

With this in view, an exploratory operation was performed by Mr. Girling Ball. Adhesions were found about the appendix, which was removed. There were numerous adhesions in the pelvis, suggestive of old tuberculous peritonitis.

Probably, therefore, the chyluria is due to a rupture of lacteals, caused by some old inflammation or abscess, in connection either with the appendix or with tuberculous glands, which has established a communication with the bladder.

*Discussion.*—Mr. GIRLING BALL said that on exploration of the abdomen it was clear that there were a large number of distended lacteals running along the internal iliac vessels on both sides of the pelvis, but more marked on the right side. Although distended, the vessels were not of great size. Smaller tributaries were seen running along the broad ligament on each side, but on being traced upwards they became lost in the retroperitoneal tissues. The cæcum was found to be bound down by adhesions to the posterior

abdominal wall; the appendix was buried amongst these adhesions; it was removed, although it seemed to have no direct connection with the lymphatics. The mesentery of the small intestine showed surface scars in several places as if they had been the seat of a chronic inflammation. The duodenum was also bound to the under surface of the liver. There were no similar adhesions on the left side of the abdomen. There was no enlargement of the lymphatic glands in the mysentery, neither was there anything of the nature of a tumour in the region of the receptaculum chyli. There was no adhesion in the pelvis, or in the neighbourhood of the ovaries. The abdomen was closed without any further procedure.

Subsequently, at a later cystoscopic examination, the aperture of the ruptured lacteal was treated by diathermic cauterization.

A month or six weeks later, on further examination, it was found that the patient was still passing the same degree of chylous fluid, but the aperture appeared to be smaller, and the stream, instead of coming in a steady flow, gushed out like a soap bubble and then burst, leaving the aperture exposed.

Dr. G. A. HARRISON said that the Sudan III came through into the urine between three and fourteen hours after it had been given by the mouth. The fat was apparently not removed by one simple extraction with ether, and it might be concluded that the opacity was not due to fat. If, however, the urine was extracted repeatedly with ether, the fat came out. The urine contained some protein, and when this was separated by boiling, the fat was also carried down. The fat in the urine was not visible under the ordinary microscope with a one-sixth objective, but with a one-twelfth objective and dark-ground illumination finely divided fat could readily be seen. The total fat amounted to only 0·1 to 0·25%, a very minute quantity, and it was surprising that there was such a marked milkiness of the urine. The patient was losing so little fat in the urine that it was insignificant from the point of view of nutrition. There was a trace of cholesterol, i.e., 3 to 9 mgm. per 100 c.c.

Dr. F. PARKES WEBER suggested that the abdominal condition in this patient was a lymphangiectatic form of congenital-developmental lymphangioma, and that the chyluria had resulted from the rupture of a vesicle projecting into the urinary bladder. In that case the chyluria might be regarded as a chylorrhagia analogous to the troublesome lymphorrhagia sometimes due to the rupture of lymphangiomatous vesicles on the surface of the body.

Dr. MORLEY FLETCHER (in reply) said that lymphangioma was improbable, especially in view of Mr. Girling Ball's findings. He did not think Dr. Parkes Weber's suggestion would account for the perforation of the bladder, the formation of the sinus, and the evidence of former peritonitis.

The frequency of micturition and incontinence of urine were present before the patient entered hospital, and these symptoms had recently increased in severity, possibly owing to the repeated cystoscopic examinations.

**Obesity. ? Cause.**—H. MORLEY FLETCHER, M.D.—S. O., schoolgirl, aged 14. Admitted to St. Bartholomew's Hospital April 29, 1929, on account of increasing obesity.

*Family History.*—Father, mother and sister alive and well. Two aunts are very fat, one weighing 13 st.

*Past History.*—Always very healthy. Pertussis and measles as a baby. Has not had scarlet fever or rheumatic fever. No head injuries or other trauma. Quite normal in height, weight, shape, intelligence, etc., until three years ago. For last three years has been putting on weight, general at first, but lately more marked over abdomen.

*Present Condition.*—Appetite not excessive. Bowels opened regularly. Headaches when constipated. Vision good. No vomiting. Micturition natural. Menstruation began at age of 11: periods irregular in onset and loss excessive. Last period December, 1928. Very fat, adiposity being equally distributed over the entire body. Body generally hairy. Hair on face: eyebrows dark. Height, 5 ft. Weight, 11 st. 3½ lb. Ears and eyes natural. Visual fields natural. Discs normal. Upper extremities fat and hairy: liniæ atrophicæ present. Chest fat: mammæ well developed. Movements

natural. Lungs and heart natural. Blood-pressure 160/130, later 130/100. Liver natural.

*Abdomen* very fat: reflexes brisk: spleen, liver, and kidneys, not palpable. No tenderness or rigidity. Many red linear scars. Distribution of hair on lower abdomen extensive and of male rather than female type.

*Lower extremities* fat and hairy: reflexes very brisk. No œdema.

*Genitalia* natural (Dr. Barris).

Dr. Fletcher's case of Obesity.

*Skiagram.*—Normal kidney shadows. This was confirmed by pyelograms by Mr. Girling Ball which showed no abnormality.

*Skiagram* of pituitary fossa and of skull generally: nothing abnormal.

*Wassermann and Sigma tests:* negative. Basal metabolic rate: + 9%. Blood-count: Red blood-cells 6,600,000 per c.mm., hæmoglobin 105%, colour-index 0·8, white blood-cells 8,400.

*Blood Sugar-curve*: slight delay; carbohydrate tolerance lowered.

*Urine and Urea-concentration Test*: normal.

The pineal and pituitary glands can probably be excluded as causative agents in this case. There are no symptoms or signs of cerebral tumour. There is no infantilism, in fact there is some degree of precocity. The mental development is normal.

*Discussion.*—Dr. BERNARD MYERS said that this might be a mixed pituitary and suprarenal case.

Dr. F. PARKES WEBER regarded the case as one of mild "inter-renalism," a term conveniently applied to cases in which there was a syndrome due to functional over-activity of the adrenal cortex, which in some lower animals constituted a separate ("inter-renal") body. In favour of his view were the masculine distribution of the pubic hair, the cutaneous striæ, the obesity, the moderate polycythæmia rubra, and the raised blood-pressure. The symptoms might be due to a tumour-like growth of the endocrine cells of the suprarenal cortex or to mere over-activity with hyperplasia of the cortex. The virilism (suggested by the pubic hair) was against the diagnosis of ovarian hyperactivity.

Dr. D. EVAN BEDFORD said that a diastolic pressure of 130 placed this case in a pathological category; it was a pathological hypertension. Such cases occurred in association with hypernephroma, and also with pituitary tumours.

Dr. TERENCE EAST said that from the appearance of the patient, her age might well be 55, instead of 14, and he regarded the case as one of ovarian deficiency. The tendency to a raised blood-pressure would agree with this condition.

Dr. F. R. B. ATKINSON said that this might be a case of thyrogenous obesity. In many such cases there were no symptoms of hypothyroidism, and the administration of thyroid then acted as a diagnostic and specific.

Dr. MORLEY FLETCHER, in reply, said he thought the cause in this case was suprarenal over-activity or a hypernephroma. This might explain the raised blood-pressure. He could not accept the idea that the case was one of ovarian or thyroid over-activity. He had postponed any specific line of treatment until the opinion of Members had been obtained.

**A Case Illustrating Putti's Anterior Bone Check Operation for Calcaneus.** — PAUL BERNARD ROTH, F.R.C.S. — D. W., a girl, aged 11, was operated on five years ago when a piece of bone was removed from the front of the left tibia and inserted into the neck of the astragalus. This piece of bone has formed a permanent projection upwards from the astragalus. When the foot dorsiflexes, this projection impinges against the lower end of the tibia, and completely prevents the calcaneus deformity.

**Von Recklinghausen's Disease.**—L. S. T. BURRELL, M.D.—A. W., male, aged 48.

*History.*—Swelling on forehead since childhood. Nodules all over body appeared 16 years ago. Patient's two brothers and maternal grandmother had similar nodules. Chronic constipation, many years, and lately symptoms of chronic pyloric obstruction with weakness and loss of weight.

*Examination.*—Very thin and cachectic-looking, with yellowish skin. Blood-pressure 90/70. Signs of chronic pyloric obstruction.

*Nodules.*—Multiple soft neuro-fibromatous nodules all over the body. Most nodules are non-pedunculated, and vary from size of a pea to that of a pigeon's egg. Some are tender on pressure, especially on extensor surfaces of forearms. Hands and feet are almost free from nodules. Largest and most numerous nodules are in region of lumbar spines and sacrum.

*Pigmentation.*—Many small areas of pale brown pigmentation all over body surface, but not on mucous membranes, varying in size from that of an ordinary freckle to that of a shilling.

Nervous, cardiac, respiratory and urinary systems appear to be normal.

*Progress.*—Asthenia, and signs and symptoms of chronic pyloric obstruction increased.

*Laparotomy* was performed, as the chronic pyloric obstruction was thought to be due to a neoplasm. It was, however, found to be caused by fibrosis following old gastric ulcers at the pyloric end of the stomach. Nothing else abnormal was found. Gastro-enterostomy was performed.

During convalescence the patient had an attack of intercostal herpes zoster, but apart from this, recovery was satisfactory.

*Pathological report on nodule from skin*: Nodule is composed of mature fibrous tissue with no sign of malignancy.

*Discussion.*—Dr. F. PARKES WEBER said that in an article by himself and Dr. J. R. Perdrau, which would shortly appear in the *Quarterly Journal of Medicine* (on neurofibromatosis), the case of a woman is described who, in addition to typical cutaneous neurofibromata ("molluscous fibromata"), had likewise periosteal and visceral neurofibromatosis, of exactly the same histological structure. (Sections from a nodule on the peritoneal surface of the ileum were examined.)

Dr. L. S. T. BURRELL, in reply, said he had looked up the literature, and he thought that if the condition proved to be one of gastric fibroma, rare though that was, this would be by no means the first case reported.

**Ascites, due to Cirrhosis of the Liver, Cured by the Talma-Morison Operation.**—CECIL P. G. WAKELEY, F.R.C.S.—C. G., male, aged 54, admitted to King's College Hospital, December 5, 1928, with very marked ascites which had been forming for three months previously. He first noticed that his ankles were swollen, in July, 1928. There was nothing of note in the past history except an operation for appendicitis in 1903.

On admission his general condition was fair; his heart was not enlarged, and the sounds were normal. Blood-pressure 165/140.

The abdomen was very swollen, and on percussion there was fluid dullness to just above the umbilicus. There was a characteristic thrill. Neither the liver nor the spleen could be palpated.

The urine was acid, and contained granular and hyalo-granular casts.

| | | | | | | |
|---|---|---|---|---|---|---|
| Urea-concentration at end of | 1st | hour | ... | 1·55 | per cent. | urea |
| ,, ,, | 2nd | ,, | ... | 1·60 | ,, | ,, |
| ,, ,, | 3rd | ,, | ... | 1·90 | ,, | ,, |

Blood-urea estimation 26 mgm. per 100 c.c.

Patient was treated with theocine sodium acetate without any benefit.

January 7, 1929.—Ascites more marked. January 13.—Slightly over 11 pints of fluid drained off the patient's legs. January 22.—47 pints of fluid drained off. Condition unchanged. February 28.—Ascites still more marked. Blood-urea 91 mgm. per 100 c.c. 40 pints of fluid drained off. March 7.—32 pints of fluid drained off. March 11.—41 pints of fluid drained off, and bandages applied to abdomen to press fluid into the feet. March 18.—Talma-Morison operation performed under gas-and-oxygen anæsthesia. A right paramedian incision exposed the peritoneal cavity, the ascitic fluid was quickly withdrawn, and the liver was found to be cirrhotic. The liver and spleen were scrubbed with gauze until the peritoneal surfaces became roughened. The omentum was then brought out of the abdomen, and sutured to the recti. The abdominal wound was closed without drainage. March 29.—Stitches were removed, wound healed and quite clean. April 17.—Blood-urea 78 mgm. per c.c. Ascites and œdema of legs gradually disappeared after several tappings.

May 21, 1929.—Left hospital to go to convalescent home.

*Present Condition.*—Patient very well; no sign of ascites or œdema of legs. Blood-urea 40 mgm. per c.c. There is a large ventral hernia in the abdominal wall, because the rectus sheath was not stitched at the operation.

Professor Rutherford Morison operated on his case (October 22, 1892), with an excellent result, and the patient returned to him two years later with a ventral hernia. An operation for this condition was followed by death in two days from some form of toxæmia. Therefore I propose to leave this patient's ventral hernia severely alone.[1]

There is no history of alcoholism in this case, but not all cases of cirrhosis are due to alcohol.

*Discussion.*—Dr. F. PARKES WEBER said he agreed that hepatic cirrhosis was certainly not always due to alcohol. The results of operative treatment of the ascites were perhaps better in the non-alcoholic cases. He thought that good results could sometimes be obtained from the ordinary omentopexy operation, not necessarily associated with the production of a ventral hernia. Paracentesis abdominis often had to be repeated at intervals for a long time after operations, so that a satisfactory result might be almost despaired of before it was ultimately obtained.

The PRESIDENT said he also was of the opinion that there was far too great a tendency to assume that a case of cirrhosis of the liver with ascites was necessarily due to alcohol. In not a few instances it certainly was not. He could understand that those cases which were not caused by alcohol would have a better prognosis than those which were, as in the former the other organs of the body were likely to be healthy, which was not the case in an alcoholic patient. That might account for some of these cases recovering so well.

**Acute Osteomyelitis treated by Diaphysectomy and Bone Grafting.**—CECIL P. G. WAKELEY, F.R.C.S.—J. N., a boy, aged 12, was admitted to hospital on September 1, 1925, with acute osteomyelitis of the left tibia, which had begun three weeks previously. His general condition was poor: temperature, 102·6; pulse, 132; respiration, 28.

The whole of the left leg was very swollen and pus was exuding from the upper end of the tibia.

Under gas-and-oxygen anæsthesia, an incision was made over the whole length of the tibia. The diaphysis of the tibia was lifted out as a sequestrum, and the wound was packed with flavine and paraffin. It healed slowly. The leg was put up in plaster, and the boy sent to a convalescent home on October 29, 1925.

He was readmitted to hospital September 29, 1926, for bone grafting, but an iodine dermatitis developed from purification, and operation was postponed.

On May 6, 1927, a large graft, 23 cm. in length, was taken from the right tibia and inserted in the left leg. Patient was discharged, in plaster, May 17, 1927.

On May 27, 1928: fitted with a weight-bearing caliper splint.

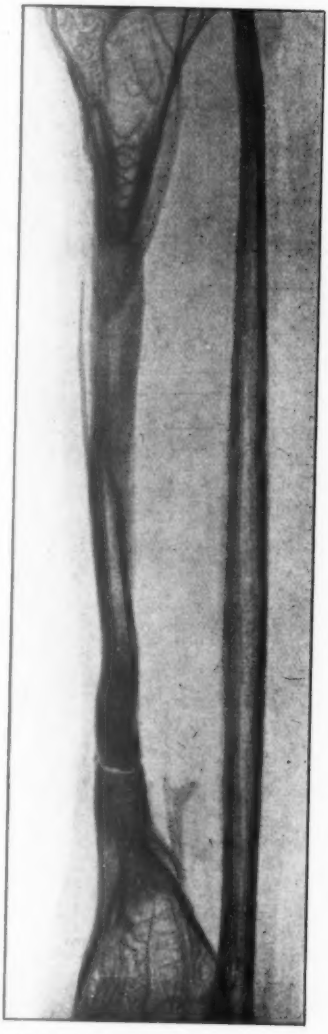
In January, 1929, while jumping over a stile he hit his left leg badly and complained of severe pain. He was brought up to hospital and examined by X-rays, when it was found that he had fractured his graft in the lower third (fig. 1).

He was treated in bed for a month, and when radiographed again, in March, 1929, the fracture of the graft was seen to have united, with much callus formation (fig. 2).

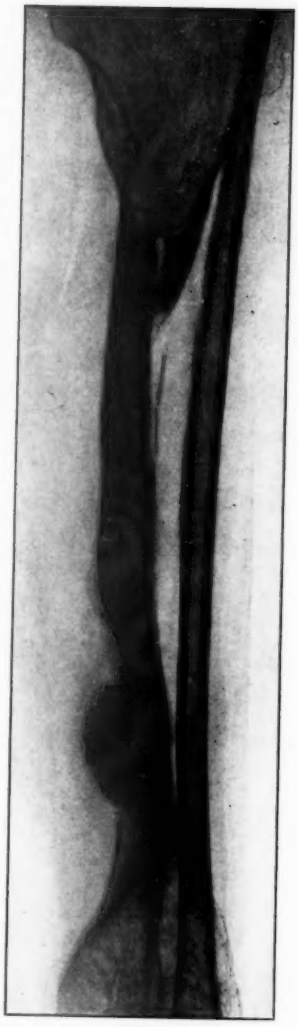
The boy is at present at school and gets about exceedingly well.

*Discussion.*—Mr. R. F. PHILLIPS asked how long the piece of bone put in was regarded as a graft. When was it considered to be part of the patient's own bone?

1 A Lister letter and a case report. *University of Durham College of Medicine Gazette*, xxvii, No. 203, 1927, p. 100.



4-1-29 FIG. 1.



5-3-29 FIG. 2.

FIG. 1.—Skiagram showing transverse fracture of graft. (Mr. Wakeley's case.)
FIG. 2.—Skiagram showing callus formation around fracture of tibial graft.

Dr. E. STOLKIND asked whether the exhibitor had ever seen cases of this kind in old people, or in adults generally. He knew a student whose left tibia was very thin, yet he played Rugby football and other games. He asked whether anything could be done in such a case.

Mr. CECIL P. G. WAKELEY (in reply) said he regarded the graft as the patient's own bone all the time. It was difficult to say when the scaffolding thrown round the graft for the formation of new bone ceased to be a mere scaffold. He thought it would be very difficult to do anything for such a case as Dr. Stolkind mentioned.

**Three Cases of Congenital Heart Disease with Cyanosis, in Adults.**—D. EVAN BEDFORD, M.D.

**I.—Fallot's Tetralogy (Pulmonary Hypoplasia with Patent Interventricular Septum and Aorta astride the Septal Defect).**—Female, aged 32. Has been blue since birth, and is always short of breath. Was first seen March, 1929, when she complained of weakness of the right leg, of a transient nature, and, later, of similar weakness of the left arm and face with numbness and tingling.

*On Examination.*—Physical development, normal. A high degree of cyanosis and clubbing of fingers and toes. Pulse often irregular from extrasystoles: blood-pressure $\frac{130}{100}$ mm. Heart not enlarged. Systolic murmur and thrill of maximum

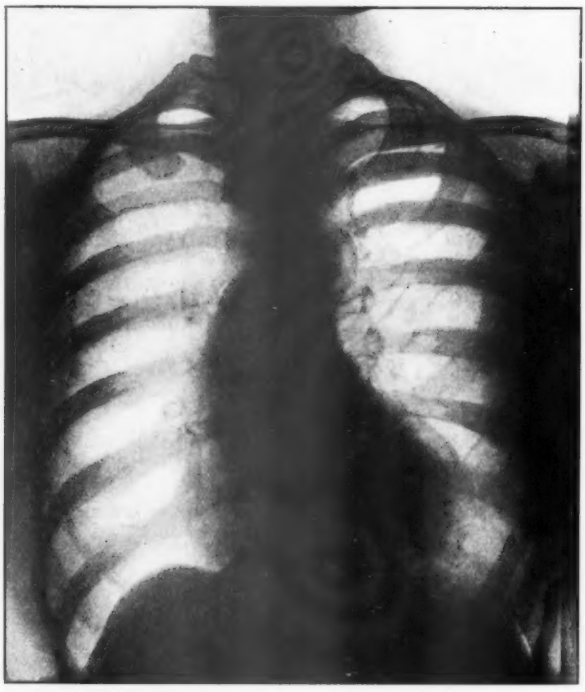


FIG. 1.—Case I. Postero-anterior radiogram. *Cœur en sabot* outline of heart. The enlargement and dextroposition of the ascending aorta, and the concavity in the region of the pulmonary artery are characteristic.

intensity in the left second and third interspaces 1 in. from sternum; thrill never intense and not always felt. Electrocardiogram shows normal rhythm and high-grade right ventricular predominance; the ventricular complexes (QRS) are of relatively large amplitude, as is common in congenital heart disease.

*Skiagram.*—Characteristic: ascending aorta projects abnormally to the right, and in position normally occupied by pulmonary artery is a noticeable concavity, indicating a small or hypoplastic vessel. Heart outline is that of so-called "cœur en sabot," apex being raised well above diaphragm level by hypertrophy of right ventricle which is seen as a convexity below the apex. This particular shape is never seen apart from congenital defects, and in acquired enlargement of the right

ventricle—for example, in Ayerza's disease—this lifting of the apex is not seen though the apex is often blunted (see fig. 1).

*Comment.*—In 1888 Fallot described a combination of congenital defects which has become known as "Fallot's Tetralogy," and which consists of the following four elements: (1) Stenosis or hypoplasia of the pulmonary artery or conus arteriosus; (2) a defect of the interventricular septum; (3) an aorta which lies astride the septal aperture and communicates with both ventricles (the "reitende aorta" of German writers); (4) great hypertrophy of the right ventricle. Not only is the aorta displaced to the right in this condition, but it is invariably wider than normal, being always enlarged when the pulmonary artery is hypoplasic. This grouping of congenital defects is far the most common cause of cyanosis and clubbing in adults. Fallot stated that it accounted for 74% of cases, judged by post-mortem findings. I would stress the point here that uncomplicated pulmonary stenosis need not cause cyanosis or marked clubbing as a rule.

A sufficient number of cases of Fallot's tetralogy has now been recorded in which clinical, radiological, and necropsy findings are available, to render the recognition of the lesion during life possible with fair certainty. Such cases have been reported by Assmann,[1] Rösler[2], Raab, Weiss and Rihl,[3] White and Sprague,[4] Arkusski,[5] and I have another radiogram of the condition in a case confirmed at necropsy.

These patients often reach adult life, and White and Sprague record the remarkable case of a distinguished American musician who attained the age of 60 and who suffered throughout his life from cyanosis, dyspnœa and other symptoms of congenital heart disease.

The main diagnostic features are as follows: (1) High-grade cyanosis and clubbing. (2) A systolic murmur and thrill at the pulmonary area or slightly below, usually of less intensity than in uncomplicated pulmonary stenosis; the thrill may be absent and the murmur slight. (3) The electrocardiogram always shows marked right ventricular predominance and often QRS waves of large amplitude. (4) The X-ray picture is characteristic and as follows: "Cœur en sabot" outline—a concavity in the region of the pulmonary artery due to hypoplasia of the vessel, though the conus arteriosus at a lower level may be dilated—visible dextroposition or enlargement of the ascending aorta. The hypoplasic pulmonary artery is important, as in uncomplicated pulmonary stenosis of the valvular type the pulmonary artery is often dilated.

**II.—Fallot's Tetralogy with a Right-sided Aortic Arch (Situs inversus Aortæ).**—Patient, female, aged 34, has been under my observation at Dr. Parkinson's clinic at the Heart Hospital for five years. Was born blue and has always been breathless. Complains of cough, dyspnœa, hoarseness, palpitation, faintness and giddiness. Eight years ago noticed a lump at the angle of the left jaw, which sometimes swells up and becomes tender.

*On Examination.*—Physical development normal. Deep cyanosis and a high degree of clubbing of fingers: the ankles and lower ends of the tibiæ are thickened. Pulse usually irregular owing to extrasystoles; blood-pressure 125/70 mm.

*Heart.*—Apex-beat in mid-clavicular line. Blowing systolic murmur, best heard in second and third interspaces to left of sternum; at times a slight systolic thrill is palpable at the pulmonary area but is inconstant. Neither murmur nor thrill is ever intense. Œdema of legs often occurs but is improved by digitalization and rest. Signs of bronchitis have often been observed. No paralysis of larynx. Electrocardiogram shows normal rhythm and ventricular extrasystoles; there is

1 Assmann, H., *Die klinische Röntgendiagnostik der inneren Erkrankungen*, Leipzig, 1928.
2 Rösler, H., *Wiener Archiv für innere Medizin*, 1928, xv, 507.
3 Raab, W., Weiss, R., and Rihl, J., *Wiener Archiv für innere Med.*, 1924, vii, 367.
4 White, P. D., and Sprague, H. B., *Journ. Amer. Med. Assoc.*, 1929, xcii, 787.
5 Arkusski, J., *Fortschr. a. d. Gebiete d. Röntgenstr.*, 1926-7, xxxv, 455.

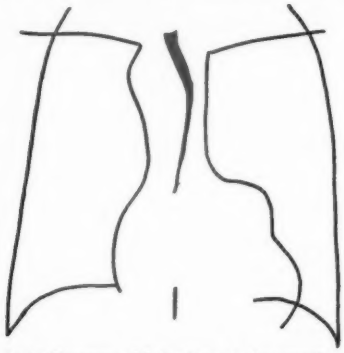


FIG. 2.—Case II. Orthodiagram with barium in the œsophagus. The normal aortic knuckle is absent on the left side, and the aortic arch lies on the right side, over the right bronchus. There is a concavity in the region of the pulmonary artery, but the conus of the right ventricle is dilated.

FIG. 3.—Case II. Second oblique position; the full width of the arch of the aorta is seen in the angle between the trachea and right bronchus, as the arch crosses the right bronchus. Barium in œsophagus.

high-grade right ventricular predominance and the QRS-waves are of large amplitude and suggestive of congenital heart disease. At the angle of the left jaw is a branchial cyst. Blood-count: Red cells 7,250,000, hæmoglobin 130%.

*Skiagram.*—Normal aortic knuckle is absent on left side and aortic arch is seen lying entirely to the right of the trachea, crossing the right bronchus. On

examination after barium has been swallowed, œsophagus is seen to lie on left of arch. This situation is absolute proof of right-sided arch in any doubtful case. In position of normal pulmonary artery is a concavity, as in the previous case; lung root-shadows are visible and indicate level of pulmonary trunk. Below this is a noticeable projection springing from the upper border of the left ventricle, and this is almost certainly a dilated conus arteriosus of the right ventricle. The apex is blunted and lies well above diaphragm level, and the right auricle is enlarged to the right. When the aorta crosses the right bronchus the appearance in the oblique positions is characteristic. In the first oblique position (half turn to the left) the full width of the arch is normally seen in front of the trachea and in the angle between the trachea and left bronchus; in the present case only a narrow strip of aortic shadow is visible owing to the trachea lying anteriorly to the arch. In the second oblique position (half turn to the right) the full width of the aortic arch is seen lying in the angle between the trachea and right bronchus, as the arch crosses the bronchus. In other words, as Assmann has pointed out, the normal appearance of the aorta in the first oblique position is seen in the second oblique position in the case of right-sided arch. (See figs. 2 and 3.)

I am indebted to Dr. Parkinson for permission to show this case.

**III.—Fallot's Tetralogy with Right-sided Aortic Arch.**—Female, aged 26. Poor physical development. She has been blue from birth, and is always breathless. Recently she has suffered from painful septic teeth, for which she sought relief at the Middlesex Hospital. Mr. Warwick James removed the teeth under ether anæsthesia, and though a good deal of bleeding from the sockets occurred, this proved beneficial to the patient.

*Examination.*—There is a high degree of cyanosis and clubbing of the fingers. The heart is not enlarged to the left. Rhythm, regular. A thrill, systolic in time, is palpable at the base of the heart; sometimes it is best felt at the pulmonary area, and sometimes over the dextroposed aorta in the first right interspace. A systolic murmur is audible over the whole præcordium, of maximum intensity in the third left interspace. The pulmonary second sound is absent.

*Radiogram* (Dr. Weinbren) shows the aorta lying to the right of the trachea and passing over the right bronchus; the normal aortic knuckle on the left is absent. In the region of the pulmonary artery there is a concavity, indicating a hypoplasic pulmonary vessel; the level of the artery is seen by the left branch forming the lung root. The apex is elevated and the right ventricle forms a part of the left heart border, giving rise to the "coeur en sabot" outline. (See fig. 4.)

*Comment.*—The marked cyanosis and clubbing in an adult and the typical clinical and X-ray signs make the diagnosis of Fallot's tetralogy fairly certain. The hypoplasia of the pulmonary artery and dilated conus arteriosus suggest a subpulmonary stenosis and a conus separated off from the main ventricular cavity, in the second case, as is quite common.

Right-sided aortic arch (*hohe Rechtslage* of German writers) may occur as an isolated malformation or may be combined with other defects. The condition is explained as a persistence of the fourth right branchial arch as the aorta instead of the fourth left arch as normally. I have observed four cases of right-sided arch and all presented clinical and X-ray signs suggestive of Fallot's tetralogy. Dr. Rösler, of Vienna, has shown me a case in which right-sided arch was the sole anomaly and was discovered by accident. The anatomy of the condition is well recognized, and is illustrated by the specimens of Mutel and Fourche.[1] After crossing the right bronchus the aorta may pass at once to the left behind the trachea and œsophagus or between them, may pass more gradually to the left, or may descend on the right. Occasionally a blind diverticulum springs from the arch behind the œsophagus, representing a persistent left aortic root; if this gives rise to

[1] Mutel and Fourche, *Bull. de la Soc. Anatom. de Paris*, 1923, xciii, 234.

the ductus arteriosus the trachea and œsophagus may be encircled and dysphagia result. A persistent left aortic root was recognized during life on X-ray examination, and confirmed at necropsy, by Arkin.[2] Another complication may arise from one of

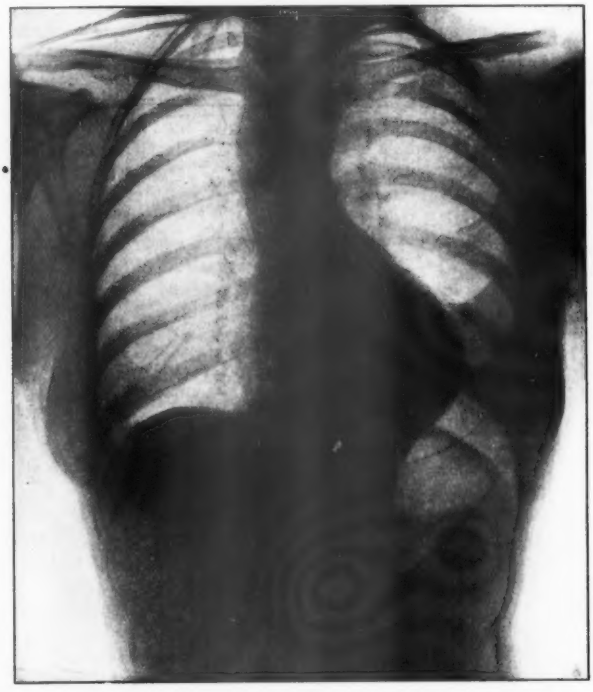


FIG. 4.—Case III. Postero-anterior radiogram. The aortic arch lies to the right of the trachea, and there is no aortic knuckle on the left. There is a concavity in the region of the pulmonary artery. *Cœur en sabot* outline of heart.

the branches of the aorta taking an aberrant course, usually the left subclavian which runs behind the trachea, and may lead to the so-called "dysphagia lusoria," as in Löweneck's case ([3]), ([4]).

**Erythræmia (Splenomegalic Polycythæmia) with a high degree of Acholuric Jaundice, probably a Manifestation of Compensatory "Hypersplenism."**—F. PARKES WEBER, M.D.

The case was published in full in the *British Medical Journal*, 1929 (ii), 892.

**Dysarthria and Abnormal Gait: Case for Diagnosis.**—F. PARKES WEBER, M.D., and O. B. BODE, M.D.

For description, see account in the *Proceedings of the Section of Neurology*, 1929, xxiii, 8.

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*The report of other cases shown at this meeting will be published in the next number of the* "PROCEEDINGS."

[2] Arkin, A., *Wiener Archiv f. inn. Med.*, 1926, xii, 385.
[3] Löweneck, M., *Fortschr. a. d. Gebiete d. Röntgenstr.*, 1926-7, xxxv, 1230.
[4] Renander, A., *Acta radiologica*, 1926, vii, 298.

# Section of Psychiatry.

President—Sir Robert Armstrong-Jones, C.B.E., M.D.

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[*November* 12, 1929.]

## PRESIDENT'S ADDRESS.

*(This address was illustrated by the collections in the Wellcome Historical Medical Museum.)*

## Superstition.

By Sir Robert Armstrong-Jones, C.B.E., M.D.

So long as darkness has existed in contrast to light, so long as moonlight has been known to man, so long as the mountain cave, the waterfall and the forest have had an interest for human beings, just so long has superstition prevailed; that is, so long has the imagination of mankind been kindled to suspect the existence of supernatural beings—gods or devils, giants and dwarfs, hobgoblins and gnomes, spirits and genii—in order to explain the actions of their daily life.

Superstition is the encroachment of faith on the rights of reason and knowledge. Superstition is founded on ignorance, and is dispelled by education, information and instruction. It is therefore the prerogative of the illiterate rather than the cultured and one of the characteristic features of primitive and savage man. Although it is more the failing of the poor and the ill-educated to believe in fortune-telling, "wise-women" and planet rulers; the wealthy and the educated not infrequently indulge in superstition, for many believe in table-turning and spirit-rapping. Indeed, some have even considered themselves to be in communication with the spiritual world.

It is difficult to explain these beliefs among sensible people, but, as we know, sensible people accept their social and political news and views from their daily papers. They abrogate their personality and believe what is told them. It is easier to believe a newspaper we read daily than a stranger, and it is easier to believe facts when they harmonize with an accepted system of knowledge, than when they are presented as isolated events. Most Christians believe in the miracles of the Bible, while they regard as superstition the belief that the blood of Saint Januarius—the patron Saint of Naples—liquefies every 19th of September. Our belief in the miracles harmonizes with the general body of the Christian doctrine, which we therefore accept.

Ordinarily, we reject supernatural stories because they do not fit in with the conclusions we ourselves have experienced, or the theories we have formed, yet fear, terror, or other emotions may compel us to believe in what we cannot prove or disprove to the satisfaction of our senses. Most of us are unconscious of the narrow range of our own experience and so involuntarily come to believe in superstition. Psychologically, this suggestion is based upon the instinct of fear, although curiosity, awe, and reverence also enter into it. It implies that the elements of

Nature, such as the sun and moon, the planets and thunder, are personified and deified and certain stones and metals or herbs come to be accredited with supernatural powers, as do charms and amulets; certain symbols and signs come to have prophetic meanings. Superstition cannot be described as an innocent mistake; it is a definite wilful belief, and this without shame, for it is a belief in what is not only contrary to the laws of Nature as generally accepted, but also contrary to experience and to common sense.

In the past, superstition related mainly to religion. The idolatry of the heathens, which is fetichism, was based upon religious belief and credulity. We read in the Scriptures that the chosen people could not be restrained from idolatry. They made the Will of God of no avail by their traditions, for they substituted ceremony in place of the religion of their fathers. Probably this custom was imitated and adopted by them from the Egyptians, with whom the Israelites sojourned for over 400 years. The Egyptians acquired their superstitions from the Persians and the Chaldeans, and we can trace superstition far back to savage and primitive man, who trepanned the skulls of the living to let out the evil spirit. They also buried their dead in sepulchres and provided the bodies with weapons of defence for their spirits after death. The Egyptians worshipped Osiris and Isis—gods representing the sun and the moon—to whom they erected temples. They also worshipped the ox or the bull—their Apis—hence, probably, the golden calf of the Jews. The Nile was personified in the crocodile and worshipped, and they also represented and worshipped the wolf, cat, dog, stork and ibis, towards which creatures they entertained superstitious legends, because they were ignorant of the laws of Nature. Comets and eclipses were regarded by the unlearned with superstition. They were signs of impending disaster, to avert which they offered sacrifices—sometimes in hundreds of victims (hecatombs)—in order to appease the Manes who were the restless spirits of their dead. For the same superstitious reasons they poured libations to their gods; they sang and danced round their altars. Sacrifices were offered to the celestial gods at sunrise and to those in the lower regions at midnight. The superstitions of the Egyptians passed on to the Greeks and Romans, but on the introduction of Christianity many of them were rooted out; Northern Europe, together with Britain, accepted the beliefs prevalent in Scandinavia and among the Gothic races, and these the Anglo-Saxons adopted. They included a belief in giants and dwarfs, in fairies, which were the personification of Providence, fays and elves of different orders, not dissimilar to the spiritual beings with human attributes which the Greeks and Romans peopled in their fields and mountains, woods and rivers. According to them the whole world was full of nymphs—some celestial, others terrestrial. The sylphs peopled the air, Shakespeare pictured the chief spirit of the air as Ariel, possibly after the angel that was cast out of heaven. He was the slave of Sycorax, and the guardian of innocence. The fauns or dryads inhabited the woods and were the patrons of wild animals. Those of the mountains were the Oreiades, of the sea the Nereides, and of the rivers, brooks and springs, the Naiades, whilst those of the valleys were Napææ. The Anglo-Saxons adopted from the Scandinavians the belief in Odin the sun and Freya the earth, and the latter corresponded to the Latin Venus. They worshipped Odin and Freya, together with their son Thor, the god of war, but they also worshipped emblems of the seasons. One of them, Eostre, was worshipped in April and has been accepted as Easter by the Christian Church. Another festival was solemnized by the burning of wood when the light of day began to lengthen in December and this we perpetuate as the Feast of the Yule log at Christmas. We also perpetuate Thor and Freya in the days of the week, as also the sun and the moon. The Anglo-Saxons believed their heroes after death, who were personified as gods, entered into Valhalla, being guided thither by twelve beautiful, but warlike nymphs, the Valkyrie.

From the introduction of Christianity in the sixth century to the middle of the seventeenth, the belief in demons—although opposed by the clergy—yet prevailed among the people. They believed in spirits, good and bad, in elves which were moving fairies. They also attributed unusual events to "lubber-fiends," which were tall, lanky, clumsy beings. The Anglo-Saxons believed in one in particular—Friar Rush, a house spirit which played domestic pranks just as Jack o' Lantern carried on outside in the fields and marshes. The Welsh believed in "Tylwyth Teg," or will of the wisp, just as the English believed in Robin Goodfellow, who did many good deeds in rural districts and was generally favoured, even by the monks. Many stories are related of the bad fairies and of the Devil's power over the priests. The fairies of the Celts were usually good little folk, regarded as diminutive beings of human appearance, perfect in form, but much more beautiful; they were so small that they could hide in flowers. The fairies were "family folk" and good neighbours, referred to as "men of peace," yet they sometimes exhibited a dwarfish malignancy. They revelled in tricks and pranks, and they often caused great trouble by kidnapping human beings—preferably unchristened infants. The stealing of children was said to be effected for the purpose of replacing some of their own numbers, as periodically they had to give up some of themselves to the master-fiend who ruled their tribes. Unfortunately, in the superstition about stolen infants, great cruelties were involved, as in order to restore the abducted child the supposititious one had to be burnt on live cinders before the real one could be returned, and children who were deformed or afflicted would often be burnt or otherwise destroyed on the plea that they were changelings, which again demonstrates the baleful effects of ignorance. Sometimes young married women were stolen or taken away in order, it was assumed, to nurse the fairies' infants; and in some parts of Ireland to-day superstition attributes maternity fatality to the evil deeds of wicked fairies. In Scotland fairies were often known as "brownies." They were small, shaggy, deformed and wild spirits, attached mostly to farmhouses, and like the fairies generally they were kind spirits and given to good deeds, whereas the evil fairies were more akin to dwarfs or the mysterious spirits described as gnomes, which lived within the earth.

It is curious that fairies were more often females than males. There were many more fairy queens than fairy kings. The domain of the fairies was underground, where the royal fairies held their court and where all was beauty and splendour. Their king was Oberon, with a crown of jewels on his head and a horn in his hand, which gave such melodious music for all to dance to on the greensward, that no mortal lips could produce the like. Their queen, Titania, was a tiny creature of surpassing loveliness. The royal fairy pageants, processions and banquets were magnificent. In processions they rode on milk-white steeds, and their dresses, always green, were rich beyond conception.

It is an easy transition—in the domain of ignorance—from a superstitious belief in good fairies, with their enchantments, to the help of evil spirits by sorcery, by which people claimed to foretell the future and to control and influence it, either by means of spells, i.e., the recitation of certain words (Abracadabra) or rubbishy sentences, or mystical formulæ described as incantations, or by the performance of certain rites or ceremonies, or the use of rings or things worn round the neck.

Sometimes the position of the planets or the stars provided the spell through astrologers. Indeed, divination by astrology was a very popular forecast, the prediction of the fortunes of individuals being based on the position of stars at the moment of birth. It is still a favourite practice. The sorcerer or soothsayer pretended to remove evil, to cure disease, or to forecast the future from the same phenomena. Occasionally spells were accomplished by the appearance of certain birds or by their flight. A single magpie is to-day believed to be an ill omen, whereas a pair brings good news. Certain birds are described as lucky, others unlucky. Swallows, storks, swans and cocks are lucky; whilst owls, ravens and

crows are unlucky, as also is the peacock, which is associated with vanity. A hare running across the path is unlucky, as also is putting on the left shoe first, the spilling of salt, and going under a ladder. Cakes are sometimes regarded with superstition. The Simnel cake is eaten in mid-Lent to commemorate the banquet given by Joseph to his brethren before they left him, and as a good omen in memory of the feeding of the 5,000.

Numbers had charms in them; number nine or three and its multiples were considered to be good omens; it was a cure for whooping-cough to pass a child under and over a donkey nine times. Many of the cures for ague, piles, whooping-cough, epilepsy, the decline, blindness and rheumatism were to be applied with the litany said nine times, the *Pater noster* nine times and incantations nine times. Snails were impaled for nine nights to cure warts, and nine pieces of elder were worn for epilepsy, while the Hydra had nine heads. Number seven was also used in charms. A cure for ague was seven sage leaves for seven mornings.

Magic writing was worn round the neck, and the Hebrews to-day have belief in their text-inscribed phylacteries. Lunacy was connected with the moon, which was believed to have a great influence over the terraqueous globe. Salt, an emblem of immortality, was a great charm, as also was rain-water on holy days. It was unlucky for the baby not to cry at its baptism, because the Devil did not get out of it. These superstitions were not wholly fanciful. They are based on some scraps of knowledge which are true and logical. Thus, the single bird implies that these birds mate for life, and to see one is to portray sorrow, separation and death. The spilling of salt is a reference to the pictures painted of the Last Supper, and walking under a ladder may have obvious results.

In Christian times the influence of the mysterious in nature was most often attributed to the fallen spirit, which was credited with a desire to do all that was evil, to carry out secret malice, to destroy all that was good in man's nature and to bring about illness or death. This influence of the evil spirit could maim and injure cattle, it could blight the crops and raise or allay storms on sea or land; but it was believed that the person exercising this power, usually an ungainly-looking old woman, had to enter into a compact with the evil one. She had to yield her body and soul to him entirely and irrevocably. The witch was controlled by the Devil and obeyed him, whilst the wizard on the other hand commanded him.

As soon as the bargain was made, the Devil gave the witch an imp, to be always at her side and to do what she willed. This imp or child was called its "familiar." The witch could assume any shape and, although most often an old woman, it was believed she, together with her imp or offspring, could fly through the air, torture her enemies, and cause irrevocable harm, yet she could vanish at will, because she could transform herself into a hare, a cat, or any other animal, and thus escape unhurt.

The compact with the Devil became of frequent occurrence, and witchcraft spread widely. It is even recorded that Cromwell, after defeating the King at the battle of Worcester on September 3, 1651, had a personal conference with the Devil and made a contract with him to secure his own will in all things for seven years. At the expiration of that period the Devil, as a part of the bargain, could have Cromwell at his sole command to do with his soul and body as was his pleasure. It was noted that seven years to the day, viz., on September 3, 1658, Oliver Cromwell died.

Superstition becomes rife and witchcraft common, well into the middle of the seventeenth century. Belief in fairies, apparitions and charms, prevailed generally throughout England, Scotland, Wales and Ireland, all such appearances being attributed to supernatural causes, i.e., they were outside and beyond the common order of Nature. Indeed, it was a mark of impiety to doubt the witch; she could inflict any evil or harm she wished, but could even do a good turn if so disposed. Her versatile methods were accepted as fact and truth. Women rather than men

were the agents of witchcraft, because it was stated a woman in the first instance and not a man yielded to the temptation of the Devil beguiled in the shape of the serpent. Both Pliny and Quintilian stated that women formed the best subjects for magical experiments.

Witchcraft probably reached its height in the sixteenth century. By this time, owing to the denunciations of Calvin and through fanatical persecution, it had spread like a plague of mental influenza over the whole of Europe, especially to Spain, Italy, France and Germany.

Many of those who confessed to witchcraft were the victims of cerebral disorder, of delusions and hallucinations, and were insane or feeble-minded. The poor wretches were conscious of unaccustomed sensations and singular promptings, and naturally referred them to the agency of demons.

Those who were described as possessed and who were called demono-maniacs were definitely insane, and they showed the type of insanity classified as *folie à deux* or communicated insanity, the morbid ideas of one person being absorbed by or conveyed to others. The treatment of the insane in the remote past was marked with great cruelty and partook greatly of superstition, and also of the nature of witchcraft, for, as Hack Tuke remarks, it was a "curious compound of pharmacy, superstition and castigation." Demoniacal possession was regarded as the chief agency in causing insanity, and exorcism was practised by the monks, who were then both priest and doctor, to get rid of the Devil. The monks also practised pharmacy, because the monastery gardens produced the medicinal herbs and plants, and thus the religious houses became the repositories of all medicines whence healing was carried out. Much superstition has continued in regard to herbs since the time of the Romans. Both Apuleius and Dioscorides, whose drawings of plants are appreciated to-day, were conscious of the healing effect of many plants, and all the early herbals support this belief. The Romans described the vervain (*herba sacra*) as the divine weed. It was used for bites of all rabid animals, and it was also prescribed to avert witchcraft and sorcery. Feasts, known as Verbenalia, were held in its honour. Rue was called the "herb of grace," and holy water was sprinkled with it to preserve health. Ophelia called it "Herb of grace o' Sundays." According to the doctrine of signatures, many plants were believed to possess the virtue of their marks or forms. The bulbous root of the pilewort (*Ranunculus ficaria*) was said to be a cure for the ailment after which it was named. The wood sorrel with its heart-shaped leaf was a cordial, the broom cured dropsy, which it actually does, and the liver-wort was a cure for liver complaints. The celandine on account of its yellow juice was a cure for jaundice, and the juice of the dandelion for warts, the eye-bright (*Euphrasia*) cured eye complaints, and lungwort (*Pulmonaria*) relieved lung symptoms, whilst the spotted herb-dragon or fritillary was an antidote to the bite of serpents. The peony as well as the hellebore were considered to be specifics for insanity, and the mugwort or wormwood cured the "devil-sickness," a mental malady "arising from a demon." Henbane was much vaunted for sleepnessness, and teucrium, probably the wood sage, was another cure for lunacy. The mandrake, a South European plant and a member of the belladonna group, whose root bore some resemblance to the human body, was prescribed for witlessness or insanity (*folie*), as was the periwinkle (*Vinca pervinca*). A radish taken by a husband the last thing at night enabled him to escape from a curtain lecture, as it stopped a woman's chatter. Polypharmacy certainly prevailed in regard to early Saxon prescriptions, and endocrinology probably had its birth in early Saxon times, for the brain of a hare or a goat, the flesh and skin of the wolf, the liver of a fowl, and the bodies of frogs, serpents and birds were prescribed; whilst eels, crabs' eyes, ants' eggs, teeth, bones and hoofs were noted as constituents in the disgusting prescriptions; but the different plants in a prescription had to be collected very often by the patient himself at certain critical hours, under a strict ritual, and to the accompaniment of

chants and psalms. Moreover, the plant ingredients, in order to be effective, had to be picked with the right hand, then passed to the left, the person was to be clad in white and be barefooted; also the moon had to be at the full or on the wane, and whilst chanting the necessary prayers almost impossible conditions were imposed which, if not observed, would be proffered as a reason for failure of the prescription to cure.

Superstition was further exemplified in the cure of insanity by immersing or "bowssening," i.e., drenching the patient in holy wells, such as the well of St. Nun, near Launceston, in Cornwall, or at St. Kea's, near Truro, or, according to Giraldus Cambrensis, at St. Winifred's in Holywell, Wales. There were several healing wells in Scotland for the cure of mental diseases, viz., one at St. Fillan's in Perthshire, one at St. Ronan's in the Butt of Lewis, and another at St. Maree in Ross-shire. The patient was looked upon as possessed by the Devil, and in order to prevent the demon lurking in the hair after immersion, the patient was plunged over head and ears into the water, and detained there (according to Sir Arthur Mitchell) almost to the point of drowning.

Another cure based on superstition was to tie an insane person to a church pillar or to a tree, where the priest, whilst flagellation or whipping the patient was being carried out, at the same time ordered the Devil to leave. Whipping or fustigation was a method of punishment approved by the saints and most grateful to them. It was believed the Devil became jealous of this method, which was thus adopted to exorcise him. Sometimes the patient would be tied to holy crosses and kept there all night, during which time prayers and incantations were uttered by the priests. In the morning the patients were well and would then be restored to liberty. It is related that a modified bridle or "brank" would in some cases be applied to the head and mouth of a noisy patient, especially if of the female sex, and the remedy was described as effective.

The healing power of stones was a great superstition among the ancients. The stones would be left with the sick person until healed, or placed in water for them to wash in. Some stones cured lameness, probably due to rheumatism, whilst others cured discharges, and others madness.

A "mad-stone," apparently a meteorite, was regarded as possessing healing powers, and there was one in Kentucky, U.S.A., and another in Carmarthen, both noted for this virtue. Superstition further extended to the use of precious stones. Many "holed" stones are known in Cornwall, Wales and Ireland to pass a limb or children through. An opal was, and still is, considered to be unlucky, because it is the eye-stone (ops). For this reason the wearer of this stone was often suspected of being a spy in the house. A ruby was an antidote to poison and also preserved the mind from evil thoughts. The diamond implied innocence, but it also indicated a strength of purpose which could not be subdued. The blue sapphire represented constancy. A pearl indicated a tear and suggested sorrow, whilst the amethyst meant joy, as it preserved inviolate the affection of the loved one. The amethyst also protected the wearer against intoxication, and drinking cups were made of it to act as a preventive charm against over-indulgence.

The "royal touch," from the time of Edward the Confessor almost to our own time, was superstitiously believed to possess healing virtues, owing to the belief in the divinity of kings. Dr. Samuel Johnson was touched by Queen Anne, and Charles II is said to have touched over 100,000 sick persons. The hope of recovery helped to raise the weakened resistance of those afflicted, demonstrating the influence of the mind on the body, which, as we know, is not a superstition. The fundamental maxim in psychology is that pleasurable sensations tend to raise all the vital functions, whilst painful sensations have the opposite effect.

Lastly, apparitions and spectral illusions easily led to superstitions about ghosts, which would give rise to curiosity and demanded an explanation. Illusions such as

the spectre of the Brocken could be explained by atmospheric conditions. As we know, ghosts occur mostly in solitary places and always at night, and these facts alone should cast suspicion on their reality. The more closely that inquiries are made to interpret the phenomena of Nature, and the more impartially that investigations are carried out to interpret them, the less support there is for any superstition concerning them and the less magic is found in them. We know to-day how frequent in bodily disorder are functional mental disturbances. Illusions, dreams and hallucinations occur in fever and after such poisons as alcohol—which can give rise to acute illusions and delirium—belladonna, henbane, opium, cannabis indica and tobacco. In remote times these would be explained as a possession by the supernatural, to-day they are natural physiological effects. The eye takes the impression, but the mind perceives; the ear hears, but the mind apprehends. Conditions formerly described as second sight or supernatural insight, brought on when the mind was in a state of frenzy, are not accepted to-day as the interpretations of the seer, but the abnormal reaction of a fevered or poisoned brain. We know to-day from the experiments of Pawlow, who has succeeded in causing the flow of saliva in dogs by means of visible signals or the hearing of bells and whistles, that an idea may be defined as a mental process which can cause chemical changes in the blood, the glands and the tissues; and *vice versa*, that the internal secretion of the ductless glands can also bring about the stimulation of an idea; in other words, an idea can alter our physical conditions just as these can vary our ideas. Ancient maxims have to-day lost their cogency, authority to-day is shaken to the core and old traditions are despised. People now do not dread the lightning, although some are killed by it, nor does the sun arouse superstitious worship of imaginary gods.

Superstition is based upon ignorance, and the more cultured and civilized a people becomes the less is the tendency to ascribe the actions of daily life to supernatural agencies.

In conclusion, let me express my sincere obligations to Dr. Charles Singer and other authorities, and in particular to the Wellcome Historical Medical Museum for supplementing the paper with demonstrations from their great and valuable collection.

# Section of the History of Medicine.

President—Dr. HERBERT R. SPENCER.

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## English Physicians in Russia in the Sixteenth and Seventeenth Centuries.

By W. J. BISHOP.

THE first practitioners of medicine in Russia—apart from the wolf-men and wizards of primitive times—were the Byzantine monks, who introduced Christianity in the tenth century, and who brought with them such knowledge of the medical and other arts as Byzantium then possessed. With the coming of Christianity the native folk-medicine received its first challenge; the new Church entered into a fierce persecution of the whole race of sages and wizards, and the use of simples was made a crime. But the popular faith in the wise-men and wise-women was not easily shaken and the lay art did not die easily. Furthermore, the monkish physicians had soon to contend with more serious rivals. As early as the eleventh century a class of foreign practitioners was in existence in Russia, the earliest of whom had come, like the monks, from Byzantium. These regular physicians by their superior skill soon gained no little reputation, and were powerfully protected by the princes and boyars, who preferred their services to those of the monks.

In the thirteenth and fourteenth centuries Russia was overrun by the Tartars, besides which plague and famine desolated the land, and during that period there was almost complete cessation of the practice of the peaceful arts. This dark age came to an end in the time of Ivan III the Great (1462-1505), under whom there was a general revival [1].

During this reign Russia was "discovered" by Europe, and there was a great influx of foreigners. Among the men of science who found their way to Moscow at this time were two physicians. The first to enter the service of Ivan, one Anthony, a German, arrived in 1483. After two years spent in the service of the Court he had his throat "cut with a knife like a sheep," for failing to cure a Tartar prince. Five years after this (1490) the second physician, Master Leo, a Venetian Jew, rashly staked his life on the cure of the Tsar's son, who suffered from a species of gout. Despite, or perhaps because of, his treatment the patient died, and the too confident doctor was publicly executed [2]. The fate of these two pioneers could scarcely have been encouraging to those who came after. Once in the Tsar's service it was not easy to leave it; and from the first the policy seems to have been "cure or be killed." But the inducements held out to foreign medical men were sufficiently strong to overcome their natural fears, and from this time onward an ever increasing number entered the service of Russia.

These immigrant physicians were men famous (or notorious) in their profession, who had been sought in many lands, and all were attached to the Court. It was only the Emperor and a few of the great lords who bestowed any confidence—and in their case it was limited—on physicians. Nothing could have induced a native-born Russian to swallow a pill, or accept any similar remedy. The usual treatment adopted by the Muscovite for any complaint was to drink a glass of

brandy, seasoned with pepper or garlick, eat a slice of onion and take a douche. The vapour baths, used in Russia from the earliest times, were also accounted a good remedy for sickness, as well as a means of cleanliness [3].

With the arrival of Richard Chancellor and his suite in Moscow in 1553 begins the story of the friendly intercourse between England and Russia that continued without interruption for three centuries. The part played in Russia by British physicians is an interesting chapter in that story, both from the points of view of general and of medical history. Many of the early physicians at the Russian Court, *e.g.*, Robert Jacob, Mark Ridley and Elisæus Bomel, were in the position of diplomatic agents, who carried on important and delicate negotiations between the two countries. "In those days when there was no resident ambassador of the one Court at the other, but only occasional missions for some special purpose, it was obviously of great advantage to an English statesman to have an intelligent, educated and observant person, such as a physician would be, residing at the Russian Court, and ready and able to keep him in touch with all that was passing there." [4]

The part played by Englishmen in the introduction and improvement of the medical art in Russia could hardly be overestimated. Many eminent medical men of other nations have entered the service of the Tsars, but there is no doubt that Englishmen (and Scotsmen) have always held a leading, and for a long time had quite the first, position. In this connection it is only necessary to mention the names of Robert Erskine, James Mounsey, Sir James Wylie, Sir Alexander Crichton and Baron Dimsdale.

The history of the rise of modern medicine in Russia—which is largely the story of the lives and work of the men we have just mentioned—has often been written. Our present purpose is to give some account of the earliest English physicians in Russia, who gained the confidence of the ferocious emperors and paved the way for a long line of successors.

## Ralph Standish (died 1559).

On the 12th of May 1557 there departed from Gravesend "foure good shippes," bearing home Ossip Grigorjevitsch Nepeja, ambassador from the Tsar Ivan the Terrible to Philip and Mary, and several Englishmen whom he had enlisted into the Tsar's service. In this company was Dr. Ralph Standish, the first English physician to enter Russia. We are fairly well informed as to the career of Ralph Standish up to the time of his departure for Russia. Matriculating from St. Nicholas Hostel, Cambridge, in 1544, he took successively the degrees of B.A. (1542-3), M.A. (1547), and M.D. (1553). He was a Fellow of Trinity College in 1548, and served the office of proctor of the University in 1551-2. Previously to this he was admitted at Gray's Inn in 1544, and appears about 1549 to have been a Registrar of the Court of Chancery. On the 5th November 1556 he was licensed by the College of Physicians to practise for one year only, and he has the distinction of being the first Licentiate on the Roll of the College [5]. Why and how this scholar-physician came to enter the service of Ivan the Terrible, and what induced him to exchange the benevolent jurisdiction of the College of Physicians for the barbarous Court of Moscow we do not know.

However, on the 13th July 1557, ambassador Nepeja arrived with the little party of Englishmen at St. Nicholas, whence they travelled by way of Colmogro and Vologhda to Moscow, which they reached on the 12th September. On the 14th September the Englishmen were received by the Emperor in state, and each of them "did his duty accordingly and kissed his right hand"; after which the Emperor bade them all welcome and commanded them to dine with him that day. The travellers had no reason to complain of their reception, and at the dinner, which lasted "about the space of five hours," they were served in vessels of gold. "As for costly meats,"

relates one of them, "he had many times seen better, but for change of wines and divers sorts of mead it was wonderful." [6]

On the 16th September the Emperor sent to each of them a "Tartarie horse to ride from place to place." On the 18th "there were given unto Master Standish, doctor in phisick, and the rest of our men of our occupations, certaine furred gownes of branched velvet and gold, and some of red damaske, of which master Doctors gowne was furred with sables." They dined again with the Emperor on the 1st October, and on five subsequent occasions, the last being on 12th April 1558. On the 10th October 1557 the Emperor gave Dr. Standish 70 roubles, and the apothecary and others each 30 roubles. This is the last reference we find to Dr. Ralph Standish, who died, probably at Moscow, within two years of entering the service of Ivan III. His will, in which he is stated to have died in foreign parts, was proved in 1559 [7].

### Richard Elmes (fl. 1557-1584).

Richard Elmes, apothecary, who went to Moscow in the same party as Dr. Standish, spent 26 years in Russia. On one occasion he incurred the wrath of the Tsar for some offence unknown to history, and only escaped a violent end through the intercession of Sir Jerome Bowes, the English ambassador at Moscow, with whom he returned to England in 1584 [8].

### Richard Reynolds (died 1606).

In 1567 Richard Reynolds (or Rainolde), a physician, Thomas Carver, an apothecary (who perished with other Englishmen in the burning of Moscow in 1571), a surgeon, and other professional men arrived in Moscow, having obtained permission of Queen Elizabeth to enter the service of Ivan the Terrible.

Richard Reynolds was of an Essex family, and was admitted a sizar of St. John's College, Cambridge, 10th November 1546, and scholar on the Lady Margaret foundation 11th November 1547. He afterwards moved to Trinity College and graduated B.A. (1549-50), M.A. (1553), and was a Fellow in 1551. On 14th March 1567 he received permission to proceed to the degree of M.D., but instead of being admitted he went with testimonial letters from the university to Russia. The careers of the emigrant Englishmen seem to have been followed with special interest by Elizabeth and her ministers, probably because many of them acted as political agents and were entrusted with secret missions. On 1st July 1568 one of the English agents wrote to Cecil, the Secretary of State, reporting the arrival of Dr. Reynolds and stating that he had been "jolyvated with 200 roubles." At the same time the apothecary received a gift of 100 and the surgeon one of 50 roubles [9].

After less than a year in Russia Reynolds returned to England and took holy orders. On 7th August 1568 he was presented by the Queen to the Rectory of Stapleford Abbots, Essex, and subsequently received two further preferments. In 1571 he was examined by the College of Physicians and "rejected as being very ignorant and unlearned; but voluntarily confessing that he had practised Physick for 2 years, the College ordered that he should be imprisoned until he had paid 20*l.*" [10].

From this time onwards he seems to have confined himself to the cure of souls, but it was not long before he again came into collision with authority. On 25th August 1579, being summoned to appear before Bishop Aylmer in St. Paul's Cathedral to answer some charge of irregularity, he assaulted the process-server and was committed to the Marshalsea. He was subsequently released, and held two of his Essex livings until his death, which took place shortly before 20th December 1606.

Richard Reynolds was the author of *A Booke called the Foundacion of Rhetorike* (1563), which was long popular, of *A Chronicle of all the Noble*

*Emperors of the Romaines* (1571), and of an Almanack and Prognostication for 1567, of which no copy is known to exist [11].

### Eliseus Bomel (died 1574).

Eliseus Bomel, son of Henry Bomel, a famous Lutheran preacher of Wesel in Westphalia, was sent to England and received his education at Cambridge. He is said to have proceeded to the degree of M.D., but there is no certain record of this. As the son of Henry Bomel and as a youth whom Philip Melancthon had "praysed highly for erudicion and godlynes," he was well received by the English reformers. In 1561 he enjoyed the patronage of Lord Mountjoy, to whom he acted as reader in the "liberal sciences," and at a later date he is said to have lived in the house of Lord Lumley [12].

Settling in London, he rapidly made a high reputation as a physician and astrologer. Strype tells us that "he was a physician of great fame, pretending to be skilled much in art, magic, and astrology," and that "people resorted to him to be cured of their sicknesses, having a wonderful confidence in him and in his magic" [13]. Sir William Cecil is said to have consulted Bomel as to the Queen's length of life, during one of the early negotiations for her marriage.

Bomel has some claim to be the original "Old Moore," for in 1567 he produced "A newe almanacke and prognostication . . . wherein is declared the right dysposition and state of the whole yeare, concerning the weather, and sicknesse comming thereof; with a prediction of such things as shall follow the terrible eclypse of the sunne this yere appearing. . . ."[1] In this—the first of the annual diaries—he details all the terrible things that were supposed to have happened after the eclipse of 1540, and foretells similar misfortunes which are only to be averted by fervent prayer [14].

In 1567 Bomel was arrested at the instance of Dr. Thomas Francis, President of the College of Physicians, for practising medicine without the Licence of the College, and was lodged in the King's Bench prison. On 25th May 1567 he wrote to Cecil, the Lord Treasurer, praying for an opportunity to expose Dr. Francis's ignorance of astronomy and Latin, and in succeeding letters he petitioned for his release and for pecuniary assistance. On 3rd May 1568 he supplicated at Oxford for incorporation as a doctor of medicine of Cambridge. In Dr. Goodall's account of the "Proceedings against Empiricks" of the College of Physicians we read that (in 1579) "the wife of one Bomelius an Empirick having procured the Lord Treasurer's letter to the College, petitioned that her husband might be discharged from prison, he having given satisfaction to the Queen's Majesty for his violation of the Statutes, in practising unlearnedly and by magical arts. To this letter the College answered, that her husband must first pay 20 *l.* for his practice and 15 *l.* for expenses in the suit, and likewise give security that he would not practise physick for the future. After this, the President of the College and Dr. Caius were appointed to wait upon Sir William Cecil (Secretary of State), he having wrote a letter to the College in favour of Bomelius; upon whose application the Secretary was pleased to express great respect of the College and all the members of it, assuring them that he should be well pleased to have Bomelius banished the kingdom. Some time after Bomelius was released from prison by consent of the College, having given bond of 100 *l.* that he would not for the future practise physick in London nor in any other parts of England" [15].

In April 1570 about the time of his release from prison, Bomel wrote to Archbishop Parker announcing that he had knowledge of a terrible danger hanging over England. The Archbishop sent the letter to Cecil, who entered into correspondence with the doctor in the expectation of discovering a conspiracy. All

[1] The only known copy of this book is in the Library of Lincoln Cathedral. Bomel appears to have issued one other edition, that licensed to Nich. Englonde in 1568/9, of which no copy is known to exist.

however that Bomel communicated to Cecil was a statement as to the Queen's nativity and a portion of a book, *De Utilitate Astrologiae*, in which he tried to prove that great changes take place every 500 years, and that as rather more than 500 years had elapsed since the Norman Conquest England must be in imminent peril. This attempt to alarm the Government and make himself of importance was unavailing, and his announcement was treated by Cecil with contempt.

While Bomel was in prison an ambassador named Ssavin, who was in London, sent him an invitation to betake himself to Russia, where he would receive good pay. With this offer Bomel now decided to close. He wrote to Cecil begging him not to throw any obstacle in the way of this project, and at the same time promised that he would supply him with political and other news and would send "annually such small presents of the produce of that extensive region as are proofs of a grateful mind." [16] Far from hindering him, the Government were probably only too glad to get rid of the doctor, and late in 1570 he returned with the ambassador Ssavin to Russia.

The subsequent career of this unfortunate adventurer is preserved in the *Travels* of Sir Jerome Horsey [17], who went to Russia in 1572. Sir Jerome frequently met Bomel at Moscow, and he writes that the doctor was then living in great pomp at the Court of Ivan Vassilovitch (IV), was in high favour as a magician, and was holding an official position in the household of the Tsar's son. He is said by Horsey to have amassed great wealth, which he transmitted by way of England to his native town of Wesel, and to have encouraged the Tsar, by his astrological mystifications and calculations, to persist in an absurd project of marrying Queen Elizabeth, making him believe "the Queen of England was younge, and that yt was very favourable for him to marry her." According to Horsey he was "an enymie alwaies to our nation" and a "practiser of much mischieff," and he seems to have exercised a malignant influence over Ivan.

After a few years of fame and prosperity Bomel was charged (about 1574) with intriguing with the kings of Poland and Sweden against the Tsar. He was arrested with others and a confession extorted from him by the rack. "The Emperor sent word they should rost him." This was done. Surviving the most diabolical tortures, he was cast into a dungeon and died there. His widow, Anne Richards, returned to England with Sir Jerome Bowes in 1584.

### Robert Jacob (died 1588).

Robert Jacob was a man of a very different stamp from the adventurer Bomel. Eldest son of Giles Jacob, of London, he was educated at Merchant Taylors' School and Trinity College, Cambridge, where he proceeded B.A. in 1569-70, was elected a Fellow, and in 1573 commenced M.A. He graduated M.D. at Basel and was incorporated at Cambridge on 15th May 1579. He became physician to Queen Elizabeth, and when in 1581 the Tsar Ivan requested the Queen to send him a skilled physician, Jacob was selected. He sailed with Sir Jerome Horsey in the summer of 1581, and the Russia Company gave him 100 roubles at his departure and maintained him at its cost until December, when Ivan Vassilovitch awarded him a salary. Dr. Jacobs afterwards gave great offence to the Company by trading in wax on his own account, whereby they suffered great loss [18]. He attended the Tsarina and acquired a reputation which long survived. Dr. Jacob recommended Lady Mary Hastings to the Tsar for his seventh wife. Happily for the lady, the Tsar died before the conclusion of the negotiations, which were opened in 1583 with the sanction of Queen Elizabeth.

After Ivan the Terrible's death early in 1584, Jacob returned to England in company with Sir Jerome Bowes and Fincham, an apothecary. On 21st May 1583 he was admitted a Licentiate of the College of Physicians, a Candidate on 12th November 1585, and a Fellow on 15th March 1586.

In August 1586 Jerome Horsey was sent to England by the new Tsar, Feodor Ivanovitch, with official despatches addressed to Elizabeth and charged with various commissions. Amongst other tasks he had to procure medical advice on certain matters, of which he writes thus:—

"I spent a good time inquiring of the learned physicians of Oxford, Cambridge, and London their opinions and directions concerning the Empress Irenia in some difficult matters relating to conception and procuration of children; she had been married seven years, and often conceived; with some other marriage matters, wherein I was charged with secrecy" [19].

Furthermore, Horsey, either out of confidence in the advice of such learned physicians as he had consulted or else mistaking his instructions, told Elizabeth that he was commissioned by the Tsar to beg that she would send a good English midwife for his consort Irenia Fedorovna. Elizabeth not only complied with this request, but also sent Dr. Jacob, her own physician, on a second journey to the Russian Court. On this occasion Elizabeth addressed the following letter to the Tsarina [20]:—

"Elizabeth . . . to the Most Gracious Orine, Empress of Russia. Most Gracious and Powerful Princess, and dearest friend and sister. The extraordinary report which has frequently reached Us of your exemplary prudence, most rare virtues and manners, truly worthy of such a Princess, which has been verbally confirmed by our physician, that worthy man, Dr. Jacobs, induces Us to love your Highness with the true affection of our soul, and ardently to wish you all possible happiness and prosperity, so that We cannot but be solicitous for your health and safety. Therefore, We have not only sent you (as you lovingly requested us) an experienced and skilful midwife to assuage the pains of childbirth by her science, but We also send you with her the aforesaid Doctor Jacob, our physician, who has been wont to take care of our health (a man previously known to you, full of faith in the medical art in which he excels), in order that he may superintend the operations of the midwife, and faithfully tend your health. We earnestly desire to be of service to Your Highness, not in this alone but in all other matters; and it will always give great pleasure to Our Sisterly mind to gratify You. Given at Our Royal Palace at Greenwich (24 March 1586)."

This assistance was not agreeable to Boris Godunov, Irenia's brother, who aspired to, and eventually usurped, the throne, to whose interest it was that the Tsarina should remain childless. The midwife was detained at Vologda, so that "the Empress never knew of her," and she was obliged to return to London in the autumn of 1587, leaving her business altogether unfulfilled.

Dr. Jacob died abroad, unmarried, in 1588.

## Baldwin Hamey (1568-1640).

The Hameys were descended from Odo de Hame, who served under the Count of Flanders at the siege of Acre. Baldwin Hamey, the elder, was born at Bruges in 1568, and studied at the university of Leyden, where he graduated M.D. In 1592 he "was sent from that university cheif physician to Theodor Ivanievitz, Emperor of Russia, with no undeserved encomium at ye request of the Muscovite Ambassador, but after a five years' honourable service and as reputable a dismission at his own request (and not without difficulty obtained too), as well as repeated importunitys afterwards from that August Court to return thither, he settled and practised 42 years in ye city of London with great reputation as an Eminent Fellow of the Royal College of Physicians there" [21].

It was in 1598 that he quitted Russia and returned to Holland, where he married at Amsterdam Sarah Oeils, and in the same year settled in London. He was admitted a Licentiate of the College of Physicians on 12th January 1610. He died from a pestilential fever, 10th November 1640, and was buried in the church of All

Hallows, Barking. His eldest son, Baldwin, became a Fellow of the College of Physicians and one of its greatest benefactors [22].

### Mark Ridley (1560-1624).

Mark Ridley, second son of Lancelot Ridley, D.D., was born in 1560 at Stretham, Cambs., of which place his father was rector. He was educated at Clare Hall, Cambridge, and graduated B.A. in 1580 and M.A. in 1584. As a Master of Arts he was admitted a Licentiate of the College of Physicians 25th September, 1590. He took the degree of M.D. in 1592, and was admitted a Fellow of the College of Physicians on 28th May 1594.

In 1594 he went to Russia as physician to the English merchants resident there, and chief physician to the Tsar Feodor I. He was chosen for the latter office by Lord Burghley, and recommended to the Tsar by Queen Elizabeth as "one of her physicians, a man learned and expert in his profession, and fit for the service of a prince." He became a great favourite at the Court and remained in Russia four years. In 1598, on the death of Feodor, he was recalled by Elizabeth. He returned to England with many compliments from the new Tsar, who promised that if in the future any English physician, apothecary, or other learned personage should desire to come to Russia, he might depend upon a kind reception, due maintenance, and a free permission to return home [23].

Dr. Ridley settled in practice in London and won an honourable position in the College of Physicians, holding successively the offices of Censor, Elect, Treasurer and Consiliarius [24]. He died early in 1624, leaving no issue. Dr. Ridley was fond of mathematics, and in 1613 published *A Short Treatise of Magneticall Bodies and Motions*, a small quarto. He claims acquaintance with William Gilbert, whom he commends for his great discoveries. In 1617 he published a book on the nature and properties of the loadstone. His portrait at the age of 34 is engraved in his *Short Treatise*.

### Timothy Willis (fl. 1615).

Timothy Willis, a doctor of medicine of Oxford and the author of two works on alchemy, was selected to succeed Mark Ridley as physician at the Russian Court in 1599. No sooner had he arrived, however, than he was sent out of the country on suspicion of political intrigue. The curious charge was brought against him that he did not bring with him a sufficient stock of books and drugs. This summary action was the occasion of a very sharp correspondence between Elizabeth and the usurper Boris Godunov, in which the Queen warmly defended the doctor [25].

### Arthur Dee (1579-1651).

With the murder of Boris Godunov in 1605 by the False Dmitri, "the Perkin Warbeck of Russia," began the "times of the troubles," and for some years Muscovy would seem to have lost its charm for English doctors. But during the reign of Michael Fedorovitch (1613-45), the first Tsar of the Romanov dynasty, the number of foreign physicians entering Russia was so great as to necessitate legislative measures for their control. A board of examination was instituted for testing the qualifications of all who desired to practise medicine in Russia. There was still a great demand for foreign talent. A contemporary traveller records that "the Russians love doctors, and medicine is in high estimation among them" [26]. The truth of this is well demonstrated in the case of Arthur Dee, son of the celebrated mathematician and astrologer, Dr. John Dee, who went out to Russia in 1627 [1].

[1] John Dee had himself received (and declined) a very flattering invitation—backed up by a promise of £2,000 yearly and "free diet from the royal kitchen"—to go and take up his residence at Moscow. (*Vide* Charlotte F. Smith's *Life of John Dee*, p. 176.)

Arthur Dee was born at Mortlake, Surrey, on 13th July 1579. He accompanied his father on his travels through Germany, Poland and Bohemia, and at an early age was initiated into the mysteries of the occult sciences. Although he did not fulfil his father's hope that he would become a "true and perfect seer," his early training resulted in a belief in alchemy and transmutation, which was maintained to the end of his life. At the age of 12 he was sent to Westminster School, and he is said by Wood to have studied subsequently at Oxford. He married, in 1602, Isabella Prestwych, daughter of Edward Prestwych, J.P., of Manchester, and began practising medicine. In his will he is described as a "Doctor of Physic" and he probably took a degree abroad [27].

About the year 1606 Arthur Dee set up in practice in London. He soon attracted the attention of the College of Physicians, for having followed a practice which, although very common at that time, was none the less adjudged "infamous conduct in a professional respect." We read in Dr. Goodall's *Account of the Proceedings against Empiricks* that Dee "was summoned before the Censors . . . he having hanged out a table, in which he exposed to sale several medicines, by which many diseases were said to be certainly cured. This crime was esteemed such an intolerable cheat and imposture that the Censors ordered him to appear with his remedies in order to the inflicting a due penalty upon him" [28]. The result of this action is not recorded.

Dee seems to have had several influential patrons. In July 1614 he was recommended by the Archbishop of Canterbury and the Lord Chancellor to be elected physician to the newly founded hospital of the Charterhouse.

In 1621—armed with a letter of introduction from King James—Dee accompanied the Ambassador Isaac Ivanovitch Pogosheff, to Moscow and became physician-in-ordinary to the Tsar Michael Fedorovitch. In 1626 he paid a visit to England, but returned to Russia in 1627 with recommendations from Charles I. He was given a house near the Ilgin Gate in Moscow and a country seat not far from the town, and for twelve years enjoyed high favour as the body-physician of the Tsar and his father, the Patriarch. His salary of 1,400 roubles a year (to which was added 72 roubles monthly for provisions, besides rations of flour, wine, mead, and oats and hay for his horses), if not comparable to that offered to his father, was at least sufficient to maintain his wife and twelve children in comfort.

During his residence at Moscow, Dee compiled a work on alchemy, which was published at Basel in 1629, and again in 1631 at Paris, under the title *Fasciculus Chemicus*. This little book was translated into English by Elias Ashmole and published with his name anagrammatized into James Hasolle (London, 1650) [29].

After the death of his wife (24th July 1634) Dee returned to England, with the highest commendations from the Tsar, and was appointed one of the physicians-in-ordinary to Charles I. He settled at Norwich, where he practised medicine with success, and became a great friend of Sir Thomas Browne. Writing to Elias Ashmole in 1658, Sir Thomas tells of the many talks he had had with "my familiar freind, sonne unto Old Doctor Dee, the Mathematician" [30]. Dee died at Norwich in September 1651, and was buried in the Church of St. George, Tomblands, in that city.

## Samuel Collins (1619-1670).

Dr. Samuel Collins is specially noteworthy as the author of *The Present State of Russia, in a Letter to a Friend at London*, a book recording his impressions formed during nine years' residence at Moscow as physician-in-ordinary to the Tsar Alexis, father of Peter the Great.

This Samuel Collins (who is not to be confused with two other seventeenth century physicians of the same names)[1] was the eldest son of Samuel Collins, vicar of Braintree, Essex, and was born in 1619. He entered Corpus Christi College, Cambridge, in 1635, but left that university without taking a degree. He afterwards graduated M.D. at Padua, and was incorporated at Oxford 5th May 1659 [31].

About the year 1660 he met, in Holland, one Gebden, a high official of the Russian Court, who was travelling to recruit men of talent for the service of the Tsar. Collins accepted Gebden's invitation to settle in Russia, and for nine years acted as physician to the Imperial Court at Moscow. He received great honours and rewards, and his fame is said to have exceeded that of all his predecessors. His last days are thus recorded in a mural inscription at Braintree Church :

"This grate was ordered to be set up by the last will and testament of Samuel Collins, late Dr. in Physick, eldest son to Mr. Samuel Collins, here under buryed, who served about eight years as principall Physician to the Great Czar, or Emperor of Russia, and after his returne from thence taking a journey into France dyed at Paris, Octr. 26th, 1670, being the 51st year of his age. Mors requies perigrinantibus" [32].

Collins's book—"*The Present State of Russia, in a Letter to a Friend at London.*" Written by an Eminent person residing at the Great Tzars Court at Mosco for the space of nine years. Illustrated with many Copper Plates"—was published in London after the author's death in 1671. It was issued in a French translation in 1679. Although the title page bears no author's name there is no doubt that it is the work of Samuel Collins. Dorman Newman, the publisher, states in a postscript that he received the manuscript from "a gentleman that attended upon the learned Dr. C. all the time of his being with the Emperor of Russia," and that the doctor's death before "it came to press" compelled him to employ "another worthy person" to edit it.

The *Present State* is a very entertaining account of life in 17th century Russia, written, in a breezy style hardly to be expected of a "learned doctor," by one who does not hide his contempt for the barbarous people amongst whom he had lived. In the course of some 140 pages the author gives his impressions of Russia, Siberia and Tartary, the land, Church and State, the people and their customs, interspersed with scandalous anecdotes of Ivan the Terrible and others, and concludes with a chapter on mushrooms. He avoided professional topics as much as possible, and it is only in two or three instances that the physician emerges, as happens when he is writing of the rigour of Russian fasts and states that "if a medicine has *Cor. cervi, ungul. Al.* or *pil. lepor.* in it, they will not take it, though to save their lives, so precise are they in observing their fasts." He thus facetiously alludes to the prevalence of venereal disease :—

"My Lady Lues Venerea is as well known in Poland as in the place where she was born ; not a *mushy panny* (Lord) nor a *pannya* (Lady) but are intimately acquainted with her, and so is the Court and the Country. The Russes, in the conquests of Vilna and many other Towns and Provinces on the Borders of Poland, have taken her ladiship prisoner, whom they are like to keep longer than their Towns. For till this war she was not known here this thousand years : But when she gets into such a cold countrey as this, she earths like a Badger so deep, that there's no driving of her out without a pickaxe or firebrand ; *juxta illud, les véroles de Rouen et la boue du Paris ne jamais sortont la pais sans oster la piece.*"

"But what is worse, the Poles have the *Plica* as familiar among them, as the French have the Itch ; and so infectious too, that few in a house escape it when 'tis once crept in amongst them. Certainly there cannot be a greater plague in the

[1] (1) Samuel Collins (1617-1685), M.D. Cambridge, Registrar of the College of Physicians.
(2) Samuel Collins (1618-1710), M.D. Padua and Oxford, President of the College of Physicians, and author of the famous *Systeme of Anatomy* (2 vols., folio, 1685).

world, for besides its many dreadful symptoms, the nasty elfish lock stinks like an old ulcer, and yet they wear it as a badge of nobility. . . . Some you shall have with hair full of brayds or knots, as I saw a monk's, which look'd like Medusa's, who for this monstrosity was accounted a man of more than ordinary sanctity. The like esteem they have of horses, who are troubled herewith in their manes, or foretops, for they think them steeds of good courage and service. If an envious person cuts off never so little of the Plica, the horse either dyes, runs mad, or becomes blind and lame."

In the last sentence Collins is referring to the popular belief that direful consequences would result from any interference with the *Plica*. This belief arose from the superstition that attributed the matted, filthy condition of the hair known as the *Plica Polonica* to the operation of wicked elves; whence also the clotted hair was often called elf-locks and elf-knots.

Shakespearians will remember that Mercutio says of Queen Mab, the fairies' midwife, in *Romeo and Juliet*:—

> "This is that very Mab
> That plats the manes of horses in the night;
> And bakes the elf-locks in foul sluttish hairs,
> Which once untangled, much misfortune bodes." [33.]

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## Edward Selleck Hare (1812-1838) and the Syndrome of Paralysis of the Cervical Sympathetic.

By J. F. FULTON, M.D.

ABSTRACT.—Edward Selleck Hare (1812-1838), the first to describe a case of cervical tumour in association with ocular symptoms (Horner's syndrome), died at the age of 26—the day before his paper was published—from typhus contracted in his wards at the Staffordshire General Infirmary. The details of his short career are described and his paper is reproduced in facsimile. He has no claim to priority over Horner, since he was not aware that the ocular symptoms in the case which he described were due to paralysis of the sympathetic.

Some months ago, while attempting to discover who had first recognized the clinical symptoms of the paralysis of the cervical sympathetic,[1] I found an important

[1] "Horner and the Syndrome of Paralysis of the Cervical Sympathetic," *Arch. of Surg.*, 1929 (April), xviii, No. 4, pp. 2025-2039.

report by "Edw. Selleck Hare, M.R.C.S., House-Surgeon to the Staffordshire County General Infirmary," addressed to the Editor of the *Medical Gazette* (London) and dated September 11, 1838. It describes the case of a man who had died of a tumour on his neck. He had for some time before death exhibited marked constriction of the left pupil and drooping of the *Levator palpebræ superioris*. Its author died on September 28, 1838, a day before the communication was published. So far as is known, he was the first clinical observer who recorded the existence of what is now termed "Horner's syndrome" in association with a cervical lesion. Hare did not speculate concerning the cause of the ocular symptoms, and one cannot, therefore, regard him as the discoverer of the symptom complex, but he made crucial clinical observations and recorded, in purely objective fashion, the details of the pathological findings, observing that many of the nerves of the neck, including the phrenic, the vagus and the whole cervical sympathetic chain, had been severely compressed, if not entirely destroyed, by the lesion.

The name of this gifted young observer is not in the *Dictionary of National Biography* or in any of the usual medical biographies or bibliographies. The only clue to his identity in his letter is his description of himself as "House-Surgeon to the Stafford County General Infirmary." A letter addressed to the secretary of the Infirmary brought a prompt and courteous reply to the effect that Dr. Hare probably took over duties at the beginning of 1837, since the Minutes of the weekly Board of January 13, 1837, are signed by him as secretary. A Minute dated October 5, 1838, made reference to his death. The following Quarterly Board granted Mrs. Hare £25 as a reimbursement of expenses incurred by Hare on behalf of the infirmary and "in testimony of the high esteem in which he was held by the Trustees of this Institution."

The circumstances and the exact date of the death of Hare have been discovered by the Manager of *The Staffordshire Advertiser*. In the issue of that journal of September 29, 1838, is a note to the effect that Mr. Hare had died of typhus on the previous day. In the same journal for the following week (October 6) there is an obituary by two medical friends. These have given me the clues by means of which I have put together some account of Hare's short career.[1]

Edward Selleck Hare, the son of James and Louisa Hare, was born at Rough Park, near Yoxall, Staffordshire, in 1812. James Hare, the father, was a farmer, and Rough Park was then the largest farm of the Stoneleigh Abbey estates, and is still in possession of Lord Leigh.[2] It appears that James Hare left Rough Park in 1814 while Edward was still an infant. From the records at University College we learn that Edward Selleck Hare came to London from Birmingham. Presumably the family had moved there after leaving Rough Park.[3] In 1832 he matriculated at University College, entering on October 4, being then aged 20. He lived at 9, Great Ormond Street, and was nominated for a place in the College by Samuel James Loyd (later Baron Overstone).

The entries in the register concerning courses taken by him are:—

4.10.32. Anatomy, Materia Medica, Chemistry.
9.10.32. Demonstrations, Surgery.
26.1.33. Anatomy, Demonstrations, Materia Medica, Chemistry, Surgery (Perpetual), Practice of Medicine.

1 I wish to acknowledge with much gratitude the generous assistance offered by the Rev. Hugh Tunnadine, Rector of Yoxall; the Rev. Luke S. Noole, Rector of Hamstall Ridware; the Rev. Lionel Lambert, Rector of St. Mary's, Stafford; Miss B. J. Orgill, of Rugeley; Mr. John Froggatt, of Rough Park Farm, and the authorities at University College, London.

2 I am indebted to him and to Mr. Francis Lees, of the Estate Office, for information and for a photograph of the house at Rough Park in which Hare was born.

3 In Robeson's *Directory* for 1839 is an entry: "Hare, James—Music smith and spring maker; Oozells Street, Broad Street, Birmingham." It is conceivable, though scarcely probable, that Edward's father had forsaken farming to become a music smith; or it is possible that the entry referred to a brother of Edward Hare whose name we know to have been also James.

4.10.33. Practice of Medicine, Midwifery.
8.10.33. Anatomy, Demonstrations, Surgery, Medical Judisprudence.
17.10.33. Botany.
28.4.34. Midwifery.

That Edward Selleck Hare gave evidence of exceptional ability as a student is shown by the following entries in the University College records :—

*Session* 1832-33.—Certificate of Honour, Class of Materia Medica and Therapeutics ; Certificate of Honour, Class of Chemistry.

*Session* 1833-34.—Second Silver Medal, Principles and Practice of Medicine ; Gold Medal and First Certificate, Class of Anatomy ; Certificate of Honour, Practical Anatomy ; Certificate of Honour, Surgery : First Silver Medal, Midwifery and Diseases of Women and Children ; Gold Medal and First Certificate, Botany.

Hare's record is certainly good, though not unique. The Gold Medal meant a first place in the class for the year ; the Silver Medal a second place. The Gold Medal and Silver Medal were not given unless a certain standard was attained, so that a man might have a first-class certificate with a medal, but not a medal without the certificate.

Hare's name appears in the list of members of the Royal College of Surgeons in 1834. He also took the licentiate of the Society of Apothecaries on July 24 of the same year. Presumably he had a hospital appointment in London or Birmingham during 1835 and 1836, and he was also married during this time. He became House Surgeon at the Staffordshire General Infirmary early in 1837, and remained there until his death nineteen months later. After his death a marble tablet was erected by subscription to his memory in St. Mary's Church, Stafford. It bears the inscription :—

EDWARD SELLECK HARE, M.R.C.S.
House Surgeon to the
Stafford County Infirmary
Died 28th Sept. 1838 aged 26 years.

Distinguished in his short career, as well
By scientific acquirement and
Professional knowledge,
As by exemplary Christian deportment ;
And early falling a sacrifice in the
Fearless discharge of professional duty ;
This tablet is erected by his
Official connections in the Infirmary
And other friends ;
In testimony of their high sense
Of his public and private worth,
Who
"By the grace of God, was, what
He was."

Hare was buried on October 2, 1838, in the graveyard of St. Mary's Church. The inscription on his tombstone is not clear enough for a photograph.

The following is the text of Hare's paper.[1]

[1] *London Med. Gaz.*, 1838, xxiii, 16-18 (n.s. vol. i).

16 TUMOR IMPLICATING THE NERVES OF THE LEFT SIDE.

## TUMOR INVOLVING CERTAIN NERVES.

*To the Editor of the Medical Gazette.*

Sir,

If you are of opinion that the points connected with physiology and pathology in the following case, render it worthy of a place in your very valuable publication, I shall be much obliged to you to give it insertion.

I am, sir, your obedient servant,

Edw. Selleck Hare, M.R.C.S.

House-Surgeon to the Stafford County General Infirmary.

September 11, 1838.

Thomas Willetts, aged 40, married, of an unhealthy complexion, was admitted to the Infirmary, under the care of Dr. Knight, on the 8th of last June. He had been attacked a month before with pain, tingling and numbness along the course of the uluar nerve of the left arm, which was most severe at the elbow, where there had also been some swelling and redness. There was, besides, pain through the left shoulder, extending across the chest to the opposite side, and upwards to the left eye and teeth of that side; also a sense of pulsation in different parts of the body, and sleepless nights. The tongue was clean, appetite good, no cough, or physical sign of pulmonary disease, and the secretions were all natural.

After a careful examination, the only cause that could be discovered to account for his symptoms was a small tumor, situated in the "inferior triangular space," on the left side of the neck, which it was possible might be producing some pressure on the origins of the nerves going to form the brachial plexus: the pulse at the wrist was equal to that of the other arm. The tumor, however, did not appear to be more than an enlarged gland, and the disease was supposed to be of a scrofulous nature.

In addition to the foregoing symptoms, the pupil of the left eye became contracted; and the levator palpebræ ceased to perform its office, the general irritability increased almost to mania, and the bowels became very torpid. In about three weeks after his admission, the pains and distressing sensations appeared to be increased, the pulse had become quicker, there were signs of debility, with numbness and coldness of the lower extremities; also by this time the tumor of the neck had become more extensive, and possessed a remarkable degree of hardness.

On the 20th of July he had almost entirely lost the power of sensation and motion in the lower extremities; and in a day or two afterwards there was a complete retention of urine. The catheter was used for about a week, when the urine again flowed, but without his being conscious of it; but he could partly empty the bladder when he chose, by the pressure of the diaphragm, scarcely, if at all, assisted by the abdominal muscles. On the 25th a slough began to make its appearance over the sacrum, but it occasioned him no pain. On the 12th of August the process of sloughing set in over each trochanter, he having been alternately laid on either side, in order to avoid the ulcer on the back. By this time the tumor of the neck had very much increased in size and prominence; the three ulcers became very extensive, and the suppuration copious; his strength gradually failed till the 26th of August, when trismus came on with paralysis of the muscles of deglutition and expectoration; and he died from suffocation at four o'clock on the following morning.

With respect to the treatment, I may observe that opiates procured him sleep, and relieved the pain without any unpleasant effect, and the eyes became more equally opened, and the pupils more symmetrical when he awoke in the morning. The repetition for a few days of exceedingly small doses of blue pill, which he took with extract of henbane, produced soreness of the gums and the mercurial breath. Leeches and blisters were repeatedly applied over the tumor, but without any effect. When the extract of belladonna was applied, the pupil of the left eye recovered its natural size for a time. Tonics and stimulants agreed, and no doubt prevented his sinking so soon as he otherwise would have done, from the inroads of the disease. For some time, also, his appetite did not fail him, and he took considerable quantities of nutritious food.

*Post-mortem inspection.*—The examination of the body was begun twenty-eight hours after death: it was now greatly emaciated. There was œdema

to a small extent in the legs and left arm.

The brain and spinal prolongation and their investing membranes were carefully examined, but no disease of any kind was detected. The optic nerves were of the same size and firmness: that portion of the medulla spinalis which swells into the cauda equina was particularly firm; there was little or no fluid in the great cavity of the arachnoid, not a large quantity in the lateral ventricles, and that in the spinal canal inconsiderable.

*Dissection of the tumor.*—After dissecting back the skin and platisma, from the left side of the neck, the superficial cervical fascia was found to be unusually dead, and the cellular tissue about it infiltrated with serous fluid. It being removed, the tumor presented its irregular surface, and was found to possess the hardness of schirrus. Some considerable veins passed into its substance, and it extended under the sterno-cleido-mastoideus and trapezius, raising on its surface the omo-hyoid, sterno-hyoid, and thyroid; which, however, were not implicated in the disease. After the removal of these the tumor was seen to extend upwards as far as the origin of the brachial plexus. The carotid artery, internal jugular vein, and pneumo-gastric nerve, passed into its substance; the first remaining pervious, the two last lost and transformed into the diseased structure, as were also the phrenic nerve, and further down the sympathetic, with its lowest cervical ganglion. The jugular vein above the tumor was atrophied, and the pneumo-gastric nerve was œdematous. The scirrhous mass extending under the clavicle, the latter was removed, and the following were its further relations:—The subclavian artery and vein passed into its substance, that portion of the anterior scalenus which separates the artery and vein, and nearly the whole of the muscle, being included in the disease, and undistinguishable. Both the artery and vein were pervious, but the latter was filled with a coagulum of a deep red colour. The tumor extended inwards as far as the trachea and arteria innominata, and downwards behind the left vena innominata and subclavian and carotid arteries, as far as the aorta, impinging upon it at the junction of its arch with the descending portion. The thoracic duct passed into and was lost in the disease, as also were the recurrent laryngeal nerve, and the veins accompanying the branches of the subclavian artery,—the branches of that artery themselves passing through the tumor without being converted into its nature. The tumor lay upon the brachial plexus, being firmly attached to the spine at the origin of the third and fourth nerves of the plexus, both which were inseparable from it.

Upon cutting into the anterior surface of the scirrhus, watery pus escaped, and the surrounding cellular tissue was œdematous. The carcinomatous mass extended itself in company with the last cervical and first dorsal nerves between the transverse processes, and into the intervertebral foramina as far as to the dura mater, which appeared beginning to be implicated; but the canal was perfect, and the appearance of the theca of the medulla not at all altered. There was no appearance of carcinoma in any other part of the body.

Observations.—The case seems to be interesting as an instance of glandular scirrhus in the male. The connexion of the disease with the distress and paralysis along the course of the ulnar and median nerves is obvious, and is evidence in confirmation of the assertion that these nerves can be traced through the plexus to the last cervical and first dorsal nerve, which I believe Boyer denies. The paralysis of the levator palpebræ, which receives a branch from the third pair; the contraction of the pupil; the pain of the teeth; the distressing sensation across the upper part of the chest; the paraplegia; the sense of pulsation in various parts of the body; and the maniacal disturbance of the mind, cannot, I apprehend, be referred to any *direct* communication between the structural disease and these several affections, but rather they must be regarded as an instance of that remote sympathy which is found to exist between distant parts of the same individual, and is most frequently displayed in persons of a nervous temperament. The œdema of the arm might possibly depend on the existence, during life, of the coagulum found in the subclavian veins; but the swelling of the elbow, which occurred at a much earlier date, could scarcely be supposed to depend on

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any impediment to the circulation at that period, and is interesting as shewing how pain and irritation of the nerves of a part, existing only sympathetically with a distant cause, may lead to structural alteration in such part, and is parallel to what occurs in hysterical females, of which I have seen many examples. The stoppage of the thoracic duct without much emaciation, perhaps is parallel to maintenance of "*embonpoint*" by hysterical patients, with the most complete anorexia for very long periods. The length of time during which the patient was bed-ridden, and the degree of emaciation and debility, taken together, were not sufficient to account, of themselves, for the sloughs over the sacrum and hip, which probably owed their existence to the paralysis of the nerves of animal life; and the fact tends to demonstrate the influence of this part of the economy over the nutritive functions.

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No one could deny the excellence of this brief clinical presentation. Just what the author intended to imply, however, by referring the ocular symptoms to "that remote sympathy which is found to exist between distant parts of the same individual" is not evident, but it is clear that he had missed the true significance of the observation. A few years later (1839) John Reid (1809-1849), the physiologist of Edinburgh, drew attention to Hare's case, and asked[1] whether injury to the sympathetic chain in man might not cause constriction of the pupil as he had found it to do in animals. Reid, however, did not find an answer to his inquiry, and the discovery remained for Horner.

1 "On the effects of lesion of the trunks of the ganglionic system of nerves in the neck upon the eyeball and its appendages," *Edin. Med. and Surg. Journ.*, 1839, lii, p. 43.

# Section of Dermatology.

President—Dr. S. Ernest Dore.

[*October* 17, 1929.]

**Monilia Infection.**—J. M. H. MacLeod, M.D.—Patient, a woman, aged 41, has onychomycosis in hands and feet. This has been present since she was a child, she believes it to be congenital.

A microscopical examination of scrapings showed a yeast-like fungus, which proved on cultivation to be *Monilia albicans*.

At present there is little inflammation around the nails, but the patient states that every now and then an inflammatory perionychia occurs, such as is familiar in monilia infections.

She had had several of the nails removed, without benefit, as the infection recurred in the new nails.

*Discussion.*—Dr. H. W. Barber asked whether the exhibitor had encountered cases of intertrigo, resembling ordinary epidermophytosis, due to *Monilia albicans*. He, the speaker, had seen a patient who gave the history that, within a few days of using a public lavatory, she developed an eruption in the groins which spread rapidly, so that when he saw her it had involved the lower abdomen, the axillæ and antecubital fossæ. A pure culture of *Monilia albicans* was obtained. The eruption was cured in two or three weeks by painting with dilute tincture of iodine.

Dr. A. M. H. Gray said he had seen a case closely resembling that described by Dr. Barber, but no culture was made. On microscopic examination the appearance was regarded as typical of that in monilia infections, namely, masses of spores with a small mycelium growth. It was acute and there was a moist dermatitis of the groins.

**Scleroderma.**—J. E. M Wigley, M.B.—Boy, aged 7½. Knocked down by bicycle four years ago. Nose bruised and swollen. Hair noticed grey in patches two years ago. Hard patches on skin of scalp and face noticed a year and a half ago. Otherwise patient is perfectly healthy.

Dr. Wigley's Case of Scleroderma.

Thickened, ivory-coloured areas of skin occupy the left cheek and side of the nose, and extend under the chin. The left ala nasi is drawn upwards and the whole side of the face appears "atrophied." Radiographic examination does not reveal any

change in the underlying bony structures. There are two similar thickened patches in the scalp. The eyelashes on the left side are white and there are many white hairs scattered over the scalp, chiefly on the left side.

There does not appear to be any loss of sensation over the patches, or any loss of muscular power on that side of the face. Physical examination reveals no other abnormality. Wassermann reaction: negative.

*Discussion.*—Dr. A. M. H. GRAY said that scleroderma was rare at the age of this patient, though it had been described even in infantile life. Three cases, he thought, had been described in infancy, and these were quite distinct from the sclerema, which was a much commoner condition in newborn infants.

Dr. F. PARKES WEBER said he thought that scleroderma of this type and distribution mostly occurred in young people and seemed always to affect both the skin and the subcutaneous tissue. He thought that a useful division of cases of localized sclerodermia was into three groups: (1) A superficial form, characterized by glossy patches, the skin only being involved; (2) cases in which both the skin and subcutaneous tissue were involved, as in the present patient; (3) a rare group of cases (apt to be wrongly diagnosed), in which there were patches of atrophy of the subcutaneous tissue (subcutaneous fat) without any real involvement of the skin (so that the term sclerodermia was really a misnomer).

**Onychomycosis.**—S. E. DORE, M.D. (President).—Patient, female, aged 54, for about a year had had an affection of the finger nails of the three middle fingers of the left hand and the ring finger of the right hand. Both thumbs are said to have been affected, but have recovered. Nails enormously thickened and opaque, yellowish in colour, raised above the nail bed, and elongated and claw-like at the ends. Toe-nails normal. Fingers thin and shrunken, apparently from disuse. No fungus found in material from nail-plate, but, on removing the projecting end of the middle finger-nail the soft, putty-like material under the nail showed abundant mycelium and spores. The pathological report stated that there was non-branching mycelium, with oval-shaped spores and budding, suggesting monilia. Cultures had so far proved negative.

The case suggests that in some instances of thickening of the nails, such as onychogryphosis, fungus might be found to be present if the nail were removed and the material beneath examined for fungus. In my experience, nails affected by ringworm are generally eroded and friable, and not hypertrophied, as in the present case.

*Discussion.*—Dr. H. C. SEMON said he thought that this condition was more common than it was usually supposed to be. He had quite recently seen a case in which the clinical manifestations gave no hint of the mycotic causation subsequently proved by the microscope. He believed that not a few of the so-called dystrophies of the nails were in reality atypical cases of tinea unguium, and that a more frequent and thorough use of the microscope would provide an increased percentage of positive results.

Dr. J. KINGSTON BARTON said it was puzzling that this disease of the nails should have existed for so many years and yet be limited to a few fingers, though it must be assumed to be contagious.

Dr. H. W. BARBER said that he had recently seen a little girl, who, for many years, had had an affection of some of her finger-nails, accompanied by a scaly eruption of the corresponding fingers; the skin of these fingers presented the curious atrophic appearance noted in this case. A pure growth of monilia was obtained in scrapings from the nails and skin. The conditions cleared up with an iodine ointment. He agreed with Dr. Kingston Barton that it was a remarkable fact that a person might have a fungus infection involving the finger- and toe-nails without any signs or history of infection of the skin.

The PRESIDENT (in reply) said that the source of infection in these cases could seldom be traced, and it was unusual to obtain any history of the infection being conveyed to others. It was surprising that there were not more cases among nursemaids who attended to children's heads, as trichophyton infections of the nails might be expected to originate in this manner.

**Milium.**—S. E. DORE, M.D.—Patient, female, aged 59, has a group of small, raised, whitish growths behind the left ear, of ten months' duration, and smaller pin-point lesions arranged in rows, which have recently appeared at the base of the neck, suggesting an affection of the sweat glands, although the recognized pathology is that it is developed from the lanugo hair follicles. Some of the larger lesions behind the ear are conical in shape, and capped by a small crust, somewhat resembling benign cystic epithelioma. Characteristic pearly milium bodies, showing concentric cells under the microscope, had been extracted from the lesions. True milium is comparatively rare, especially in this situation.

Dr. Semon saw this case previously and suggested the use of the galvano-cautery. The lesions have been treated by needling and expressing the contents.

Dr. W. N. GOLDSMITH said that he had not often seen the condition except round the eye; the grouping of the lesions in this case suggested an infective source. They appeared rather suddenly this summer and spread locally in the same way as molluscum contagiosum did, and possibly they might have a similar ætiology.

**Idiopathic Atrophy (?) Case for Diagnosis.**—J. H. T. DAVIES, M.B.—Patient, female, aged 65, has been in bad health for some time past, having had fainting attacks, breathlessness and general weakness. She had a mitral lesion and chronic myocarditis.

On the buttocks and postero-internal surfaces of the thighs are symmetrical patches of atrophy varying in size up to 4 in. in diameter. In some of the patches at a part of their circumference a patch of erythema with slight infiltration indicates the persistence of some active process. Dr. Goldsmith has just pointed out to me that the whole of the skin of the legs is similarly atrophied, a fact which I had not noticed myself.

She has felt discomfort from the cutaneous lesions on the buttocks for about two years, but cannot tell me how and when they started.

On section, the epidermis is hyperkeratotic and reduced in thickness, and the papillary line is straightened. In the papillary layer the collagen stains faintly with eosin, and is œdematous, the spaces containing a cell infiltration of small round cells and plasma cells. In the atrophic part the dermis is replaced by a structureless hyaline mass, staining a pale rose colour with van Gieson's stain and practically not at all with eosin. The elastica, which is entirely absent in these areas of hyaline degeneration and is fragmented throughout the section, seems to be heaped up at the junction of the degenerating and surviving parts of the dermis.

*Discussion.*—Dr. W. J. O'DONOVAN said he thought this was a case of lupus erythematosus. The site was extraordinary, but the clinical features of persistent erythema with fine scaling and areas of shallow scarring, where the natural cure had taken place, appeared to him to be characteristic.

The diagnosis of scleroderma had been suggested, and many cases of the association of lupus erythematosus and scleroderma in the same patient had been shown at meetings of the Section, but the atrophic areas in this case were, he thought, relics of past inflammation and not a process of scleroderma. He had seen three cases of extensive lupus erythematosus of the trunk unaccompanied by facial lesions. In particular he recalled one case of lupus erythematosus of the face which he had treated with X-rays without benefit. A fortnight after the exposure the patient maintained that this had caused an eruption of lupus erythematosus which was now visible on the inner side of one thigh.

Dr. GOLDSMITH said he thought there was no thickening in the reddened areas; on the contrary they appeared atrophic. They did not seem like the early inflammatory stage of scleroderma, in which there was usually considerable swelling of the skin. The inflamed part certainly somewhat resembled lupus erythematosus, but the atrophic areas lacked the characteristic whiteness, and there was a diffuse area behind one knee, about six inches in diameter, where the skin was thin and the veins showed through clearly, as in acrodermatitis

atrophicans. Such a diagnosis was supported by the complete disappearance of the elastic tissue. In the earlier stages of scleroderma there was hyaline degeneration of the collagen, with no involvement of the elastin.

**Idiopathic Sarcoma (Kaposi).**—J. H. T. DAVIES, M.B.—This patient, aged 48, has noticed these lesions on her legs, for about five years. Apparently they first appear in the form of the diffuse brownish stains, two of which are now present. These are mere discolorations, dotted over with minute hæmorrhages, neither the texture of the surface nor the structure of the skin being visibly or palpably altered. They are to my mind indistinguishable from Schamberg's disease. The patient complains that they itch intensely. The warty patches are all about 1 cm. by 2 cm. in size, oblong in shape and so situated on the outer surface of the lower third of the left leg as to suggest that their position is connected with some trauma inflicted by the fingers of the left hand.

They are dark brownish-purple in colour, and their appearance strongly suggests warty lichen planus.

There is I think nothing suggestive of "symmetrical purple congestion of the skin." In the latest edition of Sutton's "Diseases of the Skin" there is a coloured plate illustrating Kaposi's sarcoma and showing lesions like these.

I microscopically examined sections of one of the warty patches, and the findings are as follows: There is hypertrophy of the epidermis and papillomatosis. The papillæ are swollen and their vessels and lymph spaces are widely dilated; in many, the vascular system, which has undergone both hypertrophy and hyperplasia, as well as dilatation, seems to have arranged itself into a lobed structure, the boundaries of which are well defined by a condensation of the surrounding collagen. In the papillary layer there are bundles of newly-formed vessels similarly encapsulated, with their lumina lying parallel to the surface, in the plane contrary, in fact, to that commonly occupied by the newly-formed vessels in granulation tissue. There is very little cell infiltration. In the middle of the section there is a more dense cell infiltration which is obviously not an essential part of the neoplastic process. This infiltration ceases abruptly at a straight line separating the papillary layer from the deeper part.

In a section examined under the higher power, in one of the masses described above, there is seen an oval structure containing large irregular pale granular nuclei staining diffusely and having bright red nucleoli, which strongly suggests a Meissner corpuscle. Elsewhere in the section can be recognized other small groups of similar cells with the same spiral arrangement.

Comparison of these sections with the excellent drawings illustrating the article by MM. Pautrier and Diss, in the March number of the *British Journal of Dermatology*, strongly suggests that the condition is Kaposi's idiopathic sarcoma.

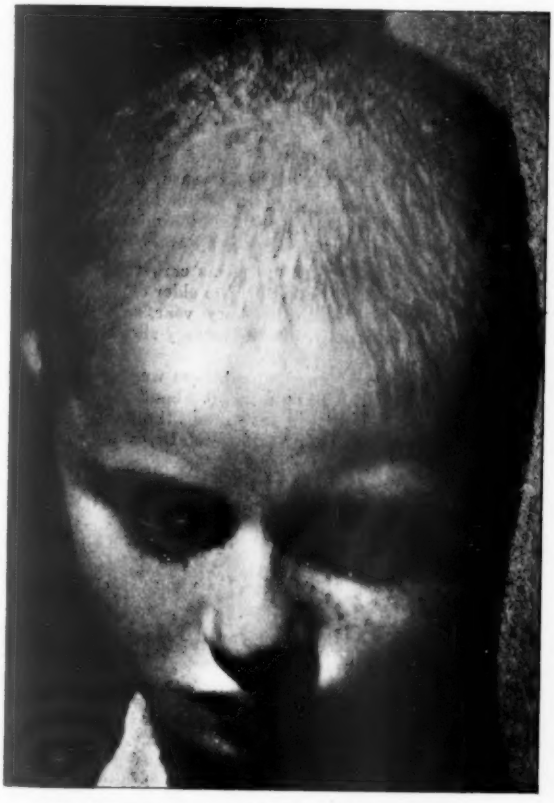
*Discussion.*—Dr. H. W. BARBER said he thought the condition was lichen planus on a varicose leg. He had recently had a case which he believed to be one of Kaposi's disease, and the histology was different from that in this case; there was a new blood-vessel formation, and the vessels had very thin walls.

The PRESIDENT said he agreed that the raised, thickened scaly patches pointed to a diagnosis of hypertrophic lichen planus.

**Idiopathic Fat Atrophy.**—R. S. RICHARDSON, L.R.C.P., M.R.C.S. (for Dr. G. B. DOWLING).—C. B., female, aged 16. Two years ago patient first noticed what she thought was a bruise on her arm. In August, 1929, she came to the West London Hospital complaining that her veins were more noticeable over the arm. On examination there was found to be atrophy of the subcutaneous tissue in three patches. Since that time these patches have increased in size and another small one has appeared.

Dr. F. PARKES WEBER thought this case was typical of his proposed third division of sclerodermia, of which he spoke earlier in the meeting, in regard to Dr. Wigley's case. Strictly, it was not scleroderma, as patches of the subcutaneous tissue (fat) were atrophied, without any involvement of the skin over them. Such cases were very rare.[1]

**Ectodermal Defect.**—R. T. BRAIN, M.D. (for Dr. W. J. O'DONOVAN).—M. F., a girl, aged 7, the child of healthy parents, has presented this defect since the age of 9 months. Before this she had a normal growth of hair. The hair of the scalp grows to a length of 1-2 cm. and then falls out. Many treatments



Dr. O'Donovan's Case of Partial Ectodermal Defect.

have been tried without appreciable effect. Patient was brought from Ireland for further advice, and admitted to the London Hospital. She is a bright, rather precocious child. The scalp is thinly covered with soft auburn hair 1-2 cm. in length, it is shorter over the occipital region, as a result of friction, but there are no bald areas suggesting alopecia. The longer hairs may be plucked out with ease and patient raises no objection.

Under the microscope the hairs show great variation in breadth and the pigment is scattered irregularly throughout their length. No abnormal fragility and no nodes

[1] Compare B. W. Howell's case, *Proc. Roy. Soc. Med.*, 1924, xvii (Section of Dermatology), pp. 72-73.

are present. No parasitic affection can be recognized. Microscopical examination of a section from the scalp reveals no definite histological abnormality. The follicles seem to be smaller than usual, and there is partial disintegration of some papillæ. There is slight round-celled infiltration of some follicles, but little more than is seen in sections of apparently normal scalps.

Remainder of skin is soft and not abnormally dry. Nails well developed. No ocular defects recognized. The teeth are small, but of good shape, although widely spaced. Heart and lungs normal. No definite evidence of hypoparathyroidism. Serum calcium 12·15 mgm. per 100 c.c. serum. Wassermann reaction, negative. Blood-count: Normal.

*Discussion.*—Dr. F. PARKES WEBER thought the title should be preceded by "congenital." "Congenital ectodermal defect" was however a term that had been appropriated for a particular group of cases, in which the skin, sweat-glands, teeth, etc., were affected (Goekermann and others).[2]

Dr. W. J. O'DONOVAN suggested that the term "ectodermal defect" was not solely applicable to the highly developed form of this congenital anomaly, but he agreed with Dr. Parkes Weber that references to this particular case, of which no similar one was recorded in the *Proceedings* of the Section, might be made under the heading of "minor ectodermal defect," as opposed to the major type, of which many striking cases had recently been reported in the *American Archives of Dermatology and Syphilology*.

Dr. A. M. H. GRAY said he had at present under his care three somewhat similar cases, two of the patients being members of one family. The elder of these two had short dry hair over parts of the scalp. It fell out regularly every year, and grew a little more each succeeding year. The other had more hair, but it was very short and dry and the lower part of the occiput was still bald.

He had shown another case of the type, in which there were two congenital bald patches, one on either side of the scalp. The curious point about the cases was the constant extensive falls of hair, followed by general improvement, the hair growing longer each time. They were not cases of ichthyosis follicularis, such as Dr. MacLeod had described some years ago.

[2] Such cases of "*combined* congenital ectodermal defect" might be called "Guilford's disease," after the describer of the first recorded case, S. H. Guilford, an American dentist, 1883.

# Section of Tropical Diseases and Parasitology.

[*November* 7, 1929.]

## Paratyphoid C an Endemic Disease of British Guiana : A Clinical and Pathological Outline. *B. paratyphosum* C as a Pyogenic Organism : Case Reports.

By GEORGE GIGLIOLI, M.D.

*B. paratyphosum* C was first isolated by Hirschfeld in the Balkan zone, during the European war, from a small number of cases of continued fever.

Since these original observations, a considerable number of case reports have, at intervals, appeared in the medical press, on sporadic occurrences of the disease, from Eastern Europe, Mesopotamia, India, China and East Africa.

From a general review of such reports little can be gathered beyond the fact that this organism is capable of determining a continued fever of the parenteric type The clinical, pathological and anatomical elements furnished are not sufficient to allow one to form an adequate idea of this disease as a clinical nosological entity, if indeed it deserves to rank as such.

The interest of these cases has in the past been mainly bacteriological; and what is more, bacteriologists appear divided in their opinion, not only concerning the validity of *B. paratyphosum* C as a species or variety, but also as to what valid species of the Salmonella or paratyphoid-enteritidis group it should be ascribed. American authors, in particular, have denied its validity and regard the term *B. paratyphosum* C as referring to miscellaneous varieties of the Salmonella group. By some it has been considered as identical with *B. aertrycke*, by others with *B. suipestifer*.

In England the important studies of Schutze, Savage and Bruce White, and Bruce White, have resulted in a well-defined typing of various members of the Salmonella group which furnishes a solid working base for the practical indentification of any given strain.

In 1920 Schutze recognized *B. paratyphosum* C as one of the types of the Salmonella group.

In 1925 Bruce White identified it with *B. suipestifer*, but in 1926 he revised his opinion, and established a *suipestifer* Hirschfeld, or *suipestifer-paratyphosus* type, based on serological and cultural characters and geographical distribution.

This type includes four subtypesit. Is not in the scope of this paper to enter into the specialized bacteriological aspect of paratyphoid C; I will limit myself to the statement that the Hirschfeld strains constitute the second, or Eastern, subtype of Bruce White's suipestifer-paratyphosus group. This includes, so far as known, only strains from human disease—from India, Mesopotamia, East Africa and the Balkans, with the exception of one strain probably imported to England from the East. The cultural characteristics of this subtype are the following: (1) Lead acetate is blackened rapidly. (2) Arabinose is fermented. (3) Dulcite is fermented. The subtype includes exclusively diaphasic strains.

I have reported elsewhere *in extenso* on my observations on paratyphoid C in British Guiana. In the limited practice of a mining camp and a poorly populated inland district, over a period of seven years I have registered no less than 135 cases, of which 80 were confirmed bacteriologically by isolation of the specific organism from the blood during life, or from the spleen post mortem. The disease appears to be endemic in the Colony, with a tendency to occasional epidemic outbursts, two of which were observed in 1924 and 1926 respectively, in coincidence with important malarial outbreaks.

The bacteriological characters of all the strains isolated coincide strictly with those given by Bruce White for his Eastern subtype of the *suipestifer-paratyphosus* group.

My findings have been confirmed by Professor Topley, to whom I am much indebted for the kindly interest with which he has followed my work.

From Professor C. Krumwiede, of the Public Health Laboratories of New York City, I have received a detailed report on a series of strains I sent him from British Guiana. While availing myself of his permission to make use of his findings, I take this opportunity of acknowledging my appreciation of his helpful assistance.

According to this authority all the Demerara strains fall into one group, presenting both specific and group agglutinogens; these do not correlate by specific and group agglutination with the stock cultures of "Hirschfeld" strains and *B. suipestifer* with which they were compared. In fact, anti-sera prepared from Guiana strains contain some agglutinins which cannot be absorbed by the stock cultures of human or porcine origin; the British Guiana strains on the other hand are unable to absorb completely the agglutinins of the stock sera. The Guiana group would therefore serologically appear as slightly different from any of the stock strains of the *B. suipestifer* group.

The occurrence and prevalence of this apparently strictly Eastern organism in British Guiana is of great interest: I have endeavoured to explain it by the very important immigratory movement to this colony from eastern countries during the past ninety years. Between 1838 and 1917 no less than 238,979 East Indian and 14,000 Chinese coolies have been imported as indentured labourers.

Whether paratyphoid C has found a particularly favourable ground in British Guiana, which has led to its assuming an endemic character, or whether the real importance of this disease has up to the present been missed in the East as it has been, and is, missed in British Guiana, is a matter which the future will decide.

I believe that as soon as hæmoculture takes its lawful place in the routine diagnosis, not only of enteric tropical fevers, but also of quinine-resistant fevers of short duration, and of that heterogeneous rubbish heap known as "P.U.O.", paratyphoid C will come to the fore as a frequent and widespread disease, calling for the same general preventive measures currently required for the other better known fevers of the enteric-parenteric group.

Paratyphoid C presents some outstanding clinical characteristics which contribute to differentiate it from other fevers of the enteric group.

It is typically—I should almost say purely—a "fever" without any special or characteristic symptom pointing to localization or preference for any particular organ or system. The temperature curve belongs in a most typical fashion to the daily remittent or daily intermittent variety. Its duration is variable; in my series of cases from five to forty days. These characters are best appreciated in cases running a protracted course. Ladder-like ascending or descending curves are common, the latter often associated with algid symptoms. In rare instances the temperature may be sustainedly high; in such cases the respiratory organs are involved through secondary inflammatory processes caused by the organisms of the respiratory tract, which take the upper hand in the conditions of diminished resistance of the patient.

Another important character of the disease is its tendency to an apyrexial course during the late stages of some of the most virulent cases. Often after a ladder-like fall to normal, the temperature will remain normal for days while the patient is evidently extremely ill and highly delirious.

Mainly on the base of these characters of the temperature curves I have divided my cases into four groups or clinical forms as follows:—

(1) Abortive and plain febrile forms of short duration, lasting from two to ten days, quinine-resistant, remittent or intermittent in character.

(2) Protracted forms, with remittent or intermittent pyrexia of long duration, from ten to forty days. The course of these cases is usually benign; in rare instances, without appearance of definite localization of the disease, the condition of the patient may gradually and progressively decline; the fever may persist or fall to normal during the latter stages of the disease. In other cases death may be due to suppurative complications, such as pyelonephritis or cholecystitis.

(3) Algid forms. The fever is high, with deep remissions to normal or subnormal, accompanied with profuse cold sweats; the hands and feet are clammy and icy cold, the patient is pulseless, anxious, restless and highly delirious; death occurs in collapse, frequently in apyrexia.

(4) Pulmonary forms, with prevalent secondary involvement of the bronchi and lungs. The physical chest-symptoms are those of plain bronchitis, lobar pneumonia, or broncho-pneumonia. Nervous symptoms are usually marked.

The epidemiological relation of paratyphoid C to malaria in British Guiana is interesting. Not only does the disease become much more prevalent in coincidence with malarial outbreaks, but its virulence increases tenfold. As the malaria curve falls, the incidence of paratyphoid C decreases and the death-rate rapidly tends to diminish. During an important epidemic of paratyphoid C, accompanying a serious outbreak of malaria in 1926, the death-rate rose to no less than 38%.

Actual association of malaria and paratyphoid C occurred in 29% of my cases.

The disease is spread mainly by contact, by patients and convalescents and presumably by healthy carriers. The importance of abortive—more or less ambulant—cases in this respect is obvious. The urine of all such persons probably constitutes the most dangerous source of infection, as bacilli are passed in very large numbers; the lack of any precaution in the disposal of urine, which, especially at night, is voided in the immediate neighbourhood of the houses, is important.

On the post-mortem table the purely septicæmic character of the disease, revealed by the clinical examination, receives anatomical confirmation. In uncomplicated cases, enlargement of the spleen, diffuse organic congestion and parenchymatous degenerations, disseminated ecchymotic effusions in the subpleural, subepicardic and subperitoneal tissue, with basal broncho-pneumonic lesions of a secondary, terminal, hypostatic character, are the only alterations found. The bowel is normal; the mesenteric glands are not altered; the size of the spleen may be enormous (5 lb.); the co-existence of acute or chronic malarial lesions may render the interpretation of the spleen findings somewhat difficult.

Post-mortem *B. paratyphosum* C can be grown easily from the spleen, liver, kidney, pancreas and adrenal; the growth is frequently very abundant. Cultures from the mesenteric gland have constantly proved negative.

Histological examination reveals diffuse congestive and degenerative parenchymatous alterations of the liver, kidney and heart muscle; the spleen shows enormous congestive engorgement and in many cases hyperplasia of the lymphatic nodes. In the liver, disseminated foci of small round-cell interstitial infiltration are frequent.

Colony-like intercellular masses of bacilli have been found in an autopsy performed four hours after death, in the liver, among the cellular trabeculæ, in the kidney, among the convuluted tubules and in the vascular tufts of the glomeruli, in the adrenals, among the cellular columns, and in the heart, among the myocardic fibres. The tissue cells appeared displaced by this growth, but not injured; no reactive inflammatory changes could be noted. *B. paratyphosum* C was the only organism obtained by culture.

This rapid and enormous multiplication must evidently be regarded as of immediate post-mortem occurrence, but it presents great interest for the explanation of the pathogenesis of the suppurative localizations of *B. paraphytosum* C which we will now consider.

By a rapid exposition of the clinical reports and post-mortem findings of the more interesting cases, I propose to illustrate the unusual characters of these suppurative conditions which contribute to mark paratyphoid C as a disease clinically different from the other fevers of the enteric group.

*Fixation Abscesses at the Site of Intramuscular Quinine-bihydrochloride Injections.*—Deep intramuscular abscesses at the site of quinine-bihydrochloride injections were observed in twenty cases. The first occurred accidentally in patients presenting a double paratyphoid-malarial infection, quinine injections having been given for the treatment of the latter condition.

I noticed that the appearance of an abscess was invariably accompanied by a marked improvement in the general condition of the patient; the dangerous septicæmic condition was cut short, fixation of the infection taking place in the *locus minoris resistentiæ* caused by the injection. Such observations induced me to resort to quinine as a provocative of fixation abscesses in all cases of paratyphoid C presenting a severe or unduly protracted course. Of fifty-nine cases in which intramuscular injections of quinine were given, either for the treatment of co-existing malaria, or for the purpose of abscess provocation, twenty developed abscesses.

The clinical features of these abscesses may be generally described as follows: The appearance of the local symptoms was constantly preceded by the fall of the temperature to normal and a very marked improvement in the patient's general condition, pointing to the onset of convalescence.

The evolution of the abscess was afebrile in 75% of the cases observed, in spite of very extensive local suppuration.

The whole process of evolution of the abscesses was practically painless and accompanied by no local subjective symptom. Patients affected with large bilateral abscesses would literally sit on them without signs of discomfort. In cases in which the abscesses had been purposely provoked, careful watch had to be kept, as the subjective symptoms would often be so slight as to be overlooked by the patient; the abscess might thus continue to evolve to an unnecessary degree without proper attention.

The anatomical appearance of the lesions, as noted during operation, was absolutely identical in all cases. The abscess was situated between the gluteus maximus and medius muscles, extending under the former in many instances to the median line. In some cases pus collections were found also, among the deeper muscles of the region. No proper, limited abscess cavity was found; the pus, which was always very abundant, filled and distended the intermuscular spaces, forming large pockets; the muscles appeared slightly œdematous, of a bright red colour. The pus was watery, of a dirty yellow-green colour, of uneven consistency, containing rag-like fibrinous masses and clots; no odour was noted.

The microscopic examination of smears showed an enormous number of highly degenerated polymorphonuclear leucocytes. Gram-negative short and long rods were constantly observed, but in varying number.

In spite of their great extent and depth, these abscesses responded rapidly to treatment and healed completely in from two to three weeks.

In only two abscess cases the patients died; both presented serious complications (bilateral pyonephrosis, and pyonephrosis and extensive bed-sores respectively). The mortality among abscess cases was 10%, while the general death-rate for all cases was 37%.

The following report refers to a typical case of fixation abscess:—

C. C., Negro labourer, aged 24, native of St. Lucia, resident in Demerara for previous four months, was admitted to hospital December 21, 1926, with a history of fever every day, with vomiting, headache, lumbar pain and cough.

On admission: Temperature 103°, pulse 29, respirations 24. Tongue slightly coated, bowels open. Spleen palpable at the costal margin. Examination otherwise negative. Blood negative for malaria parasites; urine negative for albumin.

During the first five days the fever was continuous, with a daily morning remission of two or three degrees. During the height of the fever the patient became delirious. Epistaxis occurred on the second day. There was marked dissociation between the pulse and temperature, the former rarely exceeding 96 beats per minute. The temperature became normal on the ninth day.

On the second and third day, an injection of quinine bihydrochloride of 15 gr. was given deep into the right and left buttock respectively. On the thirteenth day, after four days of apyrexia, an abscess formation was noted in the left buttock. It was not painful and not tender. There was considerable tumefaction with evident fluctuation; increase in the local heat was scarcely appreciable; there was no reddening of the skin. The patient could sit up

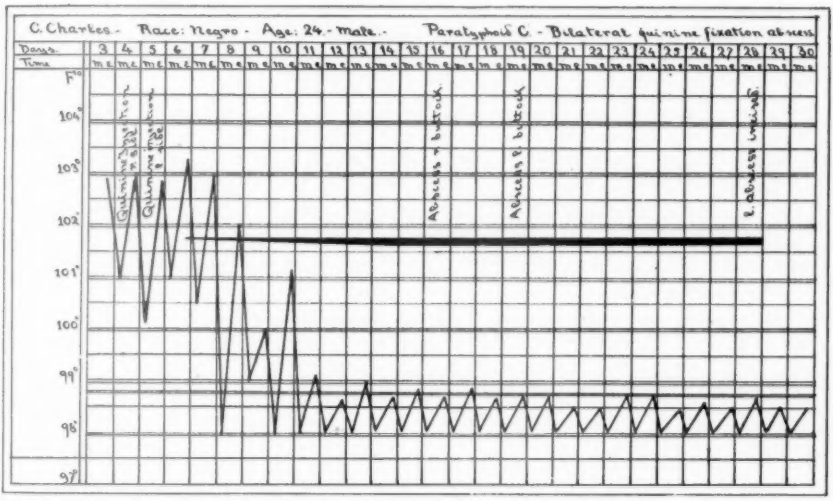



CHART I, C. C.—Paratyphoid C and double-fixation abscess of the buttock. The black bar marks the period during which suppuration was active.

in bed without discomfort. On the fourteenth day the abscess was incised. On the sixteenth day an abscess formation with identical characters became apparent in the right buttock. The abscess was allowed to evolve, but the patient's temperature remained constantly normal, while his general condition improved rapidly. On the twenty-fifth day, the right side abscess was incised. Healing of the abscesses was rapid and the subsequent course of convalescence uneventful. *B. paratyphosum* C was grown in pure culture from the pus of both abscesses.

The passage from a serious septicæmic condition to a mild local suppurative disease, following quinine intramuscular injection, was very remarkable in this case.

*Suppurative Arthritis.*—Two cases were observed in infants aged 3 and 8 months respectively. In both cases the shoulder-joint was involved.

Case No. 21.—J., a male aboriginal Indian infant, aged 3 months, admitted to hospital, April 16, 1927, with a history of fever every day and green diarrhœa for the past two weeks. He was in a marasmic condition; weight 6 lb. 12 oz.; skin dry, scaly and wrinkled. The spleen was normal. He passed four to six motions a day, of a bright green colour and mucopurulent character: no blood was seen.

On the eighth day after admission immobility of the left arm was noted; the shoulder appeared swollen, but only slightly painful to palpation and passive movement. On the following day, the local symptoms having increased, an exploratory puncture was made and pus was drawn from the joint. Arthrotomy was performed. The local condition improved rapidly, the wound appearing clean and dry at the second dressing. On the

contrary, the general condition continued to grow worse; meningitic symptoms made their appearance with a ladder-like rise of the temperature to 105°. Death supervened on the fourth day after admission.

Case No. 22.—A. A., a male child of mixed race, aged 8 years and 6 months, admitted to hospital on January 22, 1927, with a history of irregular quotidian fever during the past three weeks. The fever had ceased, but during the last two days disinclination to move the left arm had been noted by the parents. The shoulder-joint was found swollen, and the articular capsules distended; pus was drawn by exploratory puncture. Arthrotomy was performed. The child made an uninterrupted recovery, and was discharged on the sixth day to be treated as an out-patient. Healing was complete on the twelfth day and normal function was re-established one month after operation.

Smears from the pus of both the preceding cases showed Gram-negative short and long rods and culture gave a pure growth of *B. paratyphosum* C.

*Suppurated Retention Cyst of the Kidney.*

Case No. 23, D. C., an East Indian woman, aged 45, admitted on August 9, 1928, with a history of fever, headache and cough of eleven days' duration. She had been confined to her house for the last seven days in a weak condition. On August 8, though conscious, she became unable to speak and in the afternoon of the same day she became delirious.

On admission: the patient appeared in a very weak condition; could not answer questions, but did as she was told. Temperature 100·8°, pulse 104, respirations 28. Examination of the thorax revealed a diffuse bronchitis. The spleen was not palpable. The bowel function was normal. Blood-examination, negative for malaria parasites; urine, negative for albumin. Hæmoculture on the day of admission positive for *B. paratyphosum* C.

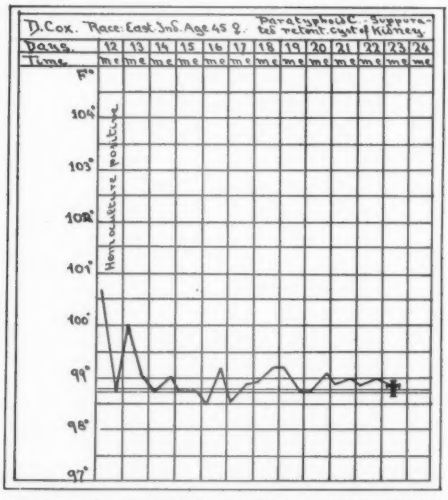



CHART II, Case No. 23.—Paratyphoid C; chronic interstitial nephritis. Suppurated retention cyst of the kidney.

On the following day the temperature fell to 99°, and from then on it became normal every morning, only rising to 99° or 99·1° in the afternoon. On the morning of August 13 the patient could speak with difficulty, in the afternoon she again lost the power of articulating, and later became delirious. During the following six days she was conscious; she was able to talk with much difficulty owing to trembling and twitching of the lips in the morning, but in the afternoon, though understanding questions, she was quite unable to answer. Her general condition grew progressively worse and she died on August 19 (twenty-third day of disease).

Post-mortem examination—showed in addition extensive other lesions of a chronic nature—numerous retention cysts in both kidneys. On the left side, on the convex surface of the organ, a tumefaction was found of the size of a small walnut. It was subcapsular and its surface was tense, fluctuating and of a yellow colour. On section it was found filled with dense, creamy yellow pus. The abscess showed a well-defined fibrous wall, with a smooth surface and the evident characters of a suppurated cyst.

*B. paratyphosum* C was grown in pure culture from the pus, which contained abundant Gram-negative rods.

*Suppurative Cholecystitis.*—Two cases were registered.

Case No. 24.—A. D., a St. Lucian, aged 19, admitted March 22, 1927, having had a daily remittent temperature for the previous ten days. His blood showed a heavy infection with *P. vivax*. Quinine treatment by mouth was instituted, and on the second day an intramuscular injection of quinine hydrochloride was administered in the left buttock.

The fever persisted, and on the fourth day *B. paratyphosum* C was isolated by hæmoculture. The temperature gradually fell, becoming normal on the twenty-fourth day after admission.

An abscess of the buttock became apparent and was incised on the thirty-fifth day. Since the fifteenth day the patient had complained of slight pain in the right hypochondrium, and a certain amount of defensive rigidity of the abdominal wall on the same side had been noted. Such symptoms persisted with a normal temperature till the fortieth day, when pain became more insistent and a tumefaction became apparent just below the costal margin on the right side. There was no jaundice. At operation a suppurative cholecystitis was found with ulceration of the fundus of the gall-bladder and a large pericholecystitic abscess. The post-operative course of this case was interesting, as the whole of the gall-bladder, with the cystic duct, sloughed out *in toto*, while the patient made a rapid and uninterrupted recovery.

*B. paratyphosum* C was grown in pure culture, from the pus, from the abscess of the buttock and from the gall bladder.

The complete evolution of both these serious suppurative complications, which, for many days, ran a parallel course, was absolutely afebrile.

Case No. 25.—H. C., a male Negro native of Dominica, residing in Demerara for the previous two years, admitted April 8, 1929, with a two-days' history of fever with persistent bilious vomiting and cough. He was in a very weak general condition, temperature 103°,

FIG. 1.—Ruptured abscess of the left lobe of the liver, from a case of double amœbic-paratyphoid C infection.

pulse 126, spleen palpable below the costal margin. The liver passed the costal margin by two inches in the nipple line. Blood, negative for malaria parasites; urine, positive for albumin. The patient died twelve hours after admission.

*Post-mortem Report*: The following are the main findings. In the lungs, old tenacious adhesions on both sides, with numerous disseminated caseous nodules in the upper lobes. Slight hypertrophy of the left ventricle of the heart, and acute dilatation of the right heart with relative insufficiency of the tricuspid valve. The spleen was four times its normal size, adherent and hard, the surface of a section presented a uniform winey red colour, the pulp being scarce. The kidneys were congested; the mesenteric glands were slightly enlarged; in the cæcum a few slightly hypertrophied solitary follicles were found; Peyer's patches in the ileum were normal. The liver was very large and heavy, with a tense capsule; the

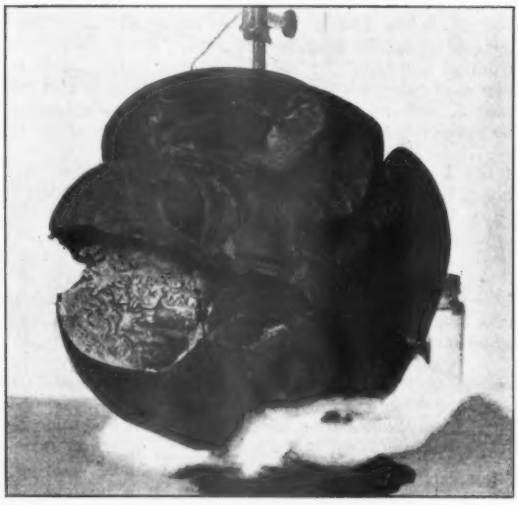


FIG. 2.—Enormous abscess of the right lobe of the liver, from a case of double amœbic-paratyphoid C infection.

surface of a section presented a uniform glassy red colour. The gall-bladder was distended and presented at its base some enlarged lymphatic glands; the fundus was slightly retracted in consequence of old adhesions; on pressure some creamy greenish pus flowed freely from the incised cystic duct. On section the organ was found distended with pus, and in proximity to the fundus, retained by a septum-like fold of the mucous membrane, caused by the old adhesions, were numerous small gall-stones.

Smears from the pus showed numerous Gram-negative short rods and *B. paratyphosum* C was grown in pure culture. Cultures from the spleen proved negative.

*Double Infection with* Entamœba histolytica *and* B. paratyphosum *C—mixed abscess of the liver.*—Two cases of mixed entamœbic-paratyphoid C infection were noted, presenting exceptional interest both for their clinical course and anatomical findings.

Case 26.—W. B., aged 29. Negro, native of St. Lucia, resident in Demerara for two years, was admitted on April 14, 1929, with a history of fever and muco-sanguinolent diarrhœa of two weeks' duration.

On admission: temperature 102·8°; pulse 96, respirations 20. Patient appeared to be ill-nourished and weak. The spleen was palpable; the liver was within its normal limits; blood negative for malaria. Patient was passing five or six muco-sanguinolent stools a day; microscopical examination showed abundance of red and white cells, but no amœbæ or cysts and no Charcot-Leyden crystals.

Hæmoculture, April 15, 1929, was negative, but a Widal test, by the culture method, gave positive agglutination for *B. paratyphosum* C (B.G. strain and No. 97 Bagdad N.C.T.S.) in a titre of 1 : 100.

The subsequent course, under symptomatic and dietetic treatment, was satisfactory. The temperature, which presented a typical daily intermittent course, gradually fell, becoming normal on the eighth day. The bowel function became normal on the fifth day. Convalescence appeared established, and continued uneventfully with isolated febrile spikes on the fourteenth and twenty-third day respectively. The patient had asked to be discharged on the twenty-fourth day; on the night of the twenty-fifth day he collapsed suddenly, dying in a few minutes. Throughout the course of the disease he never complained of abdominal or other pain.

*Autopsy* (three hours after death).—"General condition of nutrition very poor. The liver passes the costal margin by 4 in.; there is a small amount of clear free fluid in the pelvis; the visceral and parietal peritoneum are shiny; the mesenteric glands are slightly enlarged, the mesenteric fat is scarce and gelatinous. The pericardic sac contains a small amount of clear fluids; the heart is free from adhesion, is very flabby, and presents a huge engorgement and dilatation of the right cavities; the tricuspid valve is relatively insufficient, allowing the passage of three fingers; the myocardium is friable and of a dull yellowish colour. The spleen is twice its normal size, soft and flabby with a thick, wrinkled capsule; on section it presents a bright red surface on which the connective tissue

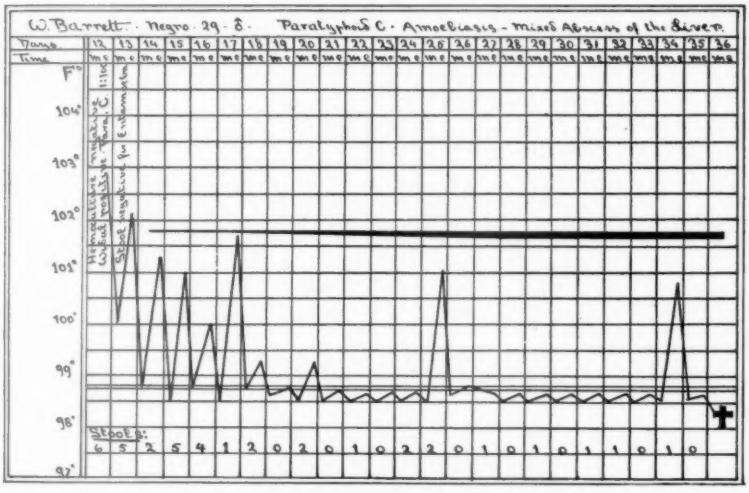



CHART III, Case No. 26.—Paratyphoid C; amœbic ulceration of the cæcum—mixed abscess of the right lobe of the liver.

structures appear markedly increased. The kidneys are congested, but otherwise normal. Nothing to note in the small bowel; on the ileo-cæcal valve is a small irregular ulcer $\frac{1}{8}$ in. in diameter, surrounded by a congested halo; the margins are clean cut and undermined. Three other similar ulcers are found in the fundus of the cæcum; the largest has a diameter of $\frac{1}{3}$ in. The liver adheres diffusely and tenaciously to the diaphragm, and to the posterior wall of the costo-lumbar sulcus. It is enlarged, weighing 4 lb. 4 oz.; and presents a large, soft, fluctuating tumefaction on the infero-posterior portion of the right lobe, deeply wedged between the vertebral column and the lower ribs, and depressing the right kidney. The wall of the tumefaction appears extremely thin towards the peritoneal cavity, being formed by little more than the capsule of the liver with a thin coating of recent fibrinous deposits. On section a large abscess cavity is opened, easily admitting both the closed fists; it is well defined and filled with greenish yellow pus, of uneven consistence, containing a very large amount of fibrinous clots and rag-like masses. There is no odour. The passage from the abscess to the normal liver tissue is gradual, through a thick zone of necrosis and another of connective tissue reaction and congestion. For the rest, the liver tissue appears intensely congested, the normal lobular structure not being evident."

Microscopic examination of the pus revealed only very few polymorphonuclear-leucocytes, and a great abundance of necrotic cellular debris and fibrinous masses. Gram-negative short bacilli were numerous, no amœbæ were found, and *B. paratyphosum* C was grown in pure culture.

Case 27.—J. R., aged 53. Negro, native of Trinidad, residing on the Demerara River, British Guiana, for previous four years, admitted March 12, 1929, fifteen days' history of quotidian fever with dysenteric symptoms.

On admission: patient's general condition was weak. He complained of severe abdominal pain, more marked in the epigastric region. He was passing from eight to ten muco-sanguinolent stools a day with much straining. Temperature 99·2°, rising to 101° at noon; pulse 96; tongue coated; abdomen moderately distended, with marked and diffuse defensive contractions which rendered palpation impossible. Marked tenderness in upper quadrants of abdomen. No vomiting; no hiccough; nothing abnormal found on examination of the various systems. The stools were very small, of a typical "currant jelly" appearance. Blood-films negative for malaria parasites. Urine positive for albumin; sediment contained abundant granular casts and white cells. Microscopic examination of the stool showed few white cells, a large number of red cells and *E. histolytica* free forms extremely abundant, very active and containing red blood-corpuscles.

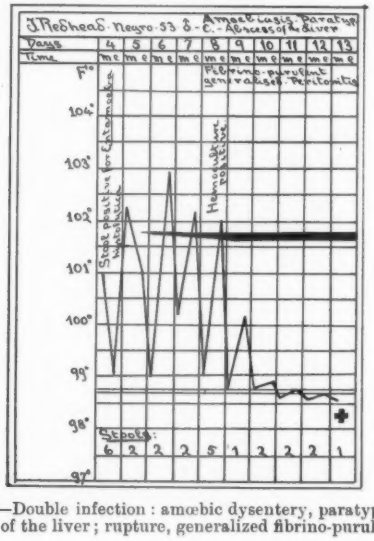



CHART IV, Case No. 27.—Double infection: amœbic dysentery, paratyphoid C. Mixed abscess of the left lobe of the liver; rupture, generalized fibrino-purulent peritonitis.

Emetine hydrochloride gr. 1 hypodermically, stovarsol gr. 4 t.i.d. and bismuth *per os* were prescribed, with hot fomentations to the epigastrium.

On the second day the dysenteric symptoms had abated (only two stools in twenty-four hours), the abdomen was partly relaxed, but defensive contraction persisted in the upper quadrants. There was less spontaneous pain and tenderness on palpation. In spite of this evident improvement, the temperature at noon ran to 102°·2, and to 103° at 4 p.m. on the third day, with a deep remission to 99° during the morning hours. On the third day the abdomen was slightly meteoric but soft, and the epigastrium was much less tender.

During the fourth and fifth days the condition remained stationary. The pulse varied from 110 to 122 with the ups and downs of the temperature. On the seventh day, emetine was stopped on account of the weak pulse, and digitalis was prescribed. The patient was quiet, but complained of sudden transitory attacks of pain in the epigastrium. Slight jaundice appeared on the fifth day, with intermittent hiccough but no vomiting. A Widal

test, carried out on the fifth day, by the cultural method, gave agglutination of *B. paratyphosum* C (British Guiana strain, and 97 Hirschfeld Bagdad N.C.T.S.) in a dilution of 1 in 100. A hæmoculture on the same date proved positive for *B. paratyphosum* C.

From the fourth day, the height of the daily afternoon febrile rises began to decline. The temperature became normal on the seventh day, and remained normal till the end. The pulse was weak, but with the fall of the fever its rate came down to 88 on the eighth day, and remained only slightly above normal to the very last.

On the seventh day an injection of quinine-bihydrochloride 10 gr. was given deep in the gluteal muscles, in the hope of producing an abscess. The general condition of the patient became progressively weaker, the features were pinched, the eyes sunken. The jaundice became more marked, and death supervened on the tenth day, immediately preceded by an attack of vomiting.

*Post-mortem Report.*—Autopsy, eight hours after death. External examination: Abdomen moderately distended, tense, the scleræ are distinctly icteric. Abdominal cavity contains a considerable amount of turbid serous fluid, in which large and small rag-like fibrino-purulent clots of a yellowish-green colour float freely. This exudate has no particular odour. The epiploön is retracted. The visceral and parietal peritoneum are opaque from recent fibrinous deposits, their blood-vessels are finely injected. The bowels are moderately distended, and the loops laxly matted together by large, soft, fibrinous clots. These are particularly abundant over the cæcum and ascending colon; in the right hypochondrium and the epigastrium the fibrinous deposits form a large solid mass which envelops completely the hepatic flexure of the colon, part of the transverse colon and the margin and lower surface of the liver.

Thorax: Lungs free from adhesions, with highly congested bases, showing numerous disseminated broncho-pneumonic foci. The heart shows marked dilatation of the right cavities; the myocardium, on section, appears of a dull yellowish colour.

Spleen small and hard, capsule thickened and coated with recent fibrinous deposits; surface of a section dark red in colour; pulp abundant; removal of pulp by gentle scraping reveals marked hyperplasia of the fibrous stroma. Kidneys slightly enlarged, flabby; capsule strips easily, revealing a number of small subcapsular cysts. On section the pelvic fat appears considerably increased; the limit between the two substances is undefined and the cortical pattern poorly visible. The small intestine appears normal in the whole of its length, with the exception of the last twenty-four inches, where one notes numerous small tumefactions protruding under the mucous membrane into the lumen of the bowel. Their size varies from that of a millet seed to that of a pea; they present a characteristic ochreous colour, and are delimited by a regular congested halo. There is no solution of continuity in the mucous membrane. A similar formation is found on the ileo-cæcal valve; Peyer's patches appear perfectly normal.

The wall of the large bowel is thickened and of uneven consistence: the mucous membrane throughout, but more especially in the cæcum, presents a large number of rounded, more or less regular ulcerations with clean-cut margins, averaging $\frac{1}{2}$ in. to $\frac{3}{4}$ in. in diameter. These ulcers appear to be in an advanced stage of healing; the fundus is clean, smooth, the margins are not undermined, and any sign of congestive or inflammatory ulcerations at the site of or around the lesions has disappeared. The contents of the bowel show no blood and only very little mucus. The mesenteric glands are normal.

For the removal of the large bowel the breaking down of the recent fibrinous adhesions in the right hypochondrium and epigastrium is necessary; a large ulcerated abscess of the lower anterior surface of the left lobe of the liver is thus uncovered. Its contents is of a greenish yellowish colour and of pultaceous consistence with abundant rag-like fibrinous masses and clots. The liver is normal in size and confirmation.

The rupture of this abscess of the liver into the general peritoneal cavity must evidently be regarded as responsible for the formidable peritoneal reaction already described.

No other abnormality found on examination of the genito-urinary organs, the adrenals, and the central nervous system.

Cultures taken eight hours after death from the free peritoneal exudate and from the abscess of the liver yielded a pure and abundant growth of *B. paratyphosum* C.

In both the preceding cases the clinical syndrome, the course of the disease and the post-mortem findings point to a primary infection of *E. histolytica* of the bowel and liver. On admission the first patient showed only suspicious dysenteric

symptoms which were not confirmed by the microscope findings. Clinically his case appeared as a plain one of paratyphoid C, and the co-existence of active amœbic disease was only revealed post-mortem in the form of four very small ulcers in the cæcum. The second case, on the contrary, appeared as a straightforward amœbic dysentery, with strong suspicions of hepatic localization (hepatitis or abscess). With emetine and stovarsol the dysentery cleared rapidly and the abdominal subjective and objective symptoms practically disappeared, while the fever on the contrary became higher and the general condition of the patient more serious. On the fourth day the character of the disease was completely changed. The progressive fall of the fever to normal, as the disease evolves to its fatal termination, is a character which I have already described as common in paratyphoid C; in spite of active suppuration in the liver and generalized fibrino-purulent peritonitis, in our second patient, the disease evolved in both cases with a normal temperature, with a pulse-rate a little above normal, without vomiting, without defensive muscular contraction of the abdominal wall, and with only the mildest subjective dolorific symptoms.

From what we have seen it is evident that *B. paratyphosum* C in British Guiana is not infrequently a cause of deep suppuration of widely varied nature.

From the history of the majority of our cases the importance of diminished local tissue vitality and resistance emerges as a primary factor in the pathology of such suppurations. This is most evident in my twenty cases of quinine fixation abscess, and in the last two cases in which, in all likelihood, an amœbic hepatitis opened the way for the localization of paratyphoid C in the liver.

In case No. 25 we have seen the infection taking advantage of a retention cyst of the kidney; in case No. 24, presumably of a cholelithiasic process; in cases 21 and 22, it is likely that some slight contusion of the shoulder-joint (of so easy occurrence among native infants) should have led the way.

Suppuration has only been observed in patients who had very recently suffered, or were actually suffering from *B. paratyphosum* C septicæmia.

In treating the general anatomical lesions in this condition I have described the widespread distribution and the abundance of the organism in the blood-stream and in all the principal organs. I have also mentioned the histological findings of colony-like masses of bacilli displacing the parenchymatous cells in the liver, kidney, adrenal, and heart muscle.

Such growth is evidently a post-mortem phenomenon, but it points to the activity with which *B. paratyphosum* C can multiply, once the vitality of the tissues has been destroyed or impaired. It is presumable that an identical process should occur among the necrosed muscular fibres of the gluteal muscles at the site of a quinine injection, or among the liver cells altered by secondary invasion of *E. histolytica* from the bowel, or in any other tissue or organ where disease of trauma should have lowered the natural power of resistance of the cells.

The bacterial invasion of the degenerated cells causes inflammatory tissue reaction, which culminates in suppuration and abscess formation.

The clinical characteristics of suppuration from *B. paratyphosum* C have already been outlined by the individual case reports, but they appear so different from the other inflammatory processes caused by the common pyogenic organisms, that it may be of advantage to conclude this paper with a short synoptic account.

(1) *B. paratyphosum* C must be regarded as an occasional pyogenic organism.

(2) Suppuration from *B. paratyphosum* C usually occurs in tissues the resistance of which has been diminished by trauma or pre-existing disease.

(3) Closed suppurative processes caused by *B. paratyphosum* C usually evolve with an apyrexial course.

(4) In suppuration from *B. paratyphosum* C the classical symptoms of inflammation (*calor, rubor, dolor, et functio læsa*) are scarcely evident. This has

been noted in all cases ranging from gluteal abscesses to generalized fibrino-purulent peritonitis.

(5) The pus is of a greenish-yellowish colour, of unhomogeneous consistence, with abundance of fibrinous rags and clots. It has no odour. Examination of smears stained by Gram's method shows abundant short and long Gram-negative rods. In many cases the bacilli are so short as to present a coccoid appearance.

(6) Suppurative lesions from *B. paratyphosum* C when appropriately surgically treated by ample incision, drainage, and dry aseptic plugging of the cavity, heal rapidly and easily.

*Discussion.*—Dr. H. SCHÜTZE said that in 1918 Ledingham had noticed, in his Mesopotamian cases, the frequency with which abscesses occurred in association with paratyphoid C; these abscesses were found in the liver and kidney and were characteristically multiple, a feature which served to differentiate them from those of amœbic dysentery. Pulmonary complications were also a feature of the cases.

Mackie and Bowen reported finding multiple abscesses in the liver and an abscess in the buttock from which the bacillus of paratyphoid C was isolated; they remarked upon the particular liability of paratyphoid C to produce visceral infection, especially in the lungs.

Mr. BRUCE WHITE said that Dr. Giglioli's paper added further evidence to support an opinion that paratyphoid C is in the main a secondary disease, depending sometimes on debilitating conditions (anæmia, scurvy, neoplasms), but more frequently superimposed on pre-existing protozoal or typhus infection. In the Russian epidemics (1921-23) of paratyphoid C the infection spread almost exclusively among those suffering from, or convalescing from, relapsing fever, though in a few cases typhus played the primary rôle. Summing sixty-five case records of paratyphoid C infection furnished by Neukirch (Turkey), Dienes and Wagner (Galicia), Hirschfeld (Balkans), Bosch (Sumatra), and Garrow (East Africa) it was found that twenty-one sufferers had malaria, five showed spirochætes in their blood, and two (? three) had or had had typhus.

There was a distinct parallel between the secondary rôle of Hirschfeld's organism in human disease and that of the *Bacillus suipestifer* in hog-cholera; in view of the specially close serological—and presumed genetic—relation of these organisms, this point had an added interest.

It was probable that the barrier to the spread of Hirschfeld's organism in Western Europe was the absence of a widespread protozoal or virus disease of man affording it a pathogenic opportunity.

## The Epidemiology and Pathology of Tuberculosis in India.

[Abstract of a paper read by A. C. UKIL (Calcutta).]

AN attempt has been made to discover the causes of the rapidly increasing morbidity and mortality from pulmonary tuberculosis in India. The methods employed in study were: (1) A tuberculin survey (cutaneous test with pure tuberculin) of 6,500 persons in rural, semi-rural and urban areas in four provinces; (2) the mortality statistics; (3) a study of the clinical forms of the disease and of post-mortem lesions; (4) isolation and typing of strains of tubercle bacilli from extra-pulmonary lesions; (5) a study of the rôle of secondary bacterial flora in phthisis in the tropics, and (6) a consideration of certain metabolic factors and the influence of climate and of sunlight on the incidence of the disease.

The average incidence of cuti-reaction over all ages was found to be 33·4% for rural, 47·9% for semi-rural, and 55·1% for urban areas. Variations in the frequency and the intensity of the reaction have been studied. As studied from the mortality curves, hospital and necropsy returns, and other evidences, the peak of mortality curve in infancy and childhood, as found in Europe, was lacking. The open-air life of the people and the raising of immunity by exposure to sunlight have been suggested as possible causes.

The presence of imperfect specific immunity in the population has been shown by cuti-reaction figures, and post-mortem data from hospital cases and cases of accidental deaths, and has been compared with data in European countries. Massive infection being extremely frequent, this factor, operating on an imperfectly immunized soil, explains most of the clinical and pathological lesions met with. A study of the secondary bacterial flora (aerobic and anaerobic) has brought out the fact that, apart from their ulcerative action in cavities, they increase the virulence of the tubercle bacilli in many cases.

It has further been shown that extra-pulmonary tuberculosis in India is almost entirely due to the human type of tubercle bacillus.

[The paper was discussed by Dr. Haslam, Dr. Graham Forbes, Dr. Christopherson and others.]

# Section of Electro-Therapeutics.

President—Dr. C. A. ROBINSON.

[*October* 18, 1929.]

## PRESIDENT'S ADDRESS.

## Diathermy Treatment of Puerperal Septicæmia and Pneumonia.

By C. A. ROBINSON, M.B.

THE subject of electro-therapy has suffered in the past—and is still suffering—from the want of sufficient test of the efficiency of our work. A knowledge of physics, of machines, of the chemical and physical effects produced by electrical currents and of the physiological results is very desirable, but what we really want to know is the effect on diseased conditions or on persons affected by disease. This we can find out only by empirical observation—by a system of trial and error.

To illustrate my contention I shall make use of work which is especially familiar to me and much of which is peculiarly my own.

The history of electro-therapeutics up to the end of last century provides little of practical value for us. One reason for this is that before about 1880, quantities of electricity used in treatment were not measured. Useful work had undoubtedly been done with the faradic current, but this is difficult to measure; it may, of course, be measured by the use of standard coils. These were and still are used in physiological experiments but it is doubtful if they were used for purposes of treatment. Probably the current was only measured then, as it is now, for clinical applications, by its effects upon the patient. Another reason is that in assessing the truth of claims made for the results of treatment, the following postulates were not satisfied :—

1. There must be a diagnosis of the existing pathological conditions, or a syndrome sufficiently constant for the cases to be classified, in order that the results observed may be comparable.

2. A record of progress must be kept. It is desirable that some physical or chemical phenomenon should be quantitatively recorded, especially if it can be put into the form of a curve. Some definite observable facts such as the range of movement of a joint, variation in the temperature, the condition on intrapelvic examination, or pulse and respiration frequency—to mention only a few—should be available.

3. The history of the cases after cessation of treatment should be stated when possible. This, however, is often difficult to obtain.

4. The results of the treatment must be capable of being repeated with a certainty which varies only with variations in the nature of the cases or in the completeness with which the treatment is carried out.

5. To these must be added the specification of the quantity of current used, with the size of electrodes or some other quantitative indication of effect, such, for instance, as may be derived from the sensations of the patient.

I do not say that no good can be done unless all these postulates are satisfied; but we must deplore the fact that so little attempt has hitherto been made to fulfil them. We must deplore the lack of scientific clinical investigation.

Let me take as an example the claims made for the treatment of dysmenorrhœa by diathermy. Dysmenorrhœa is little more than a symptom. For the present purpose, we may roughly divide cases of dysmenorrhœa into two classes: (1) the so-called "spasmodic dysmenorrhœa," and (2) that due to inflammation of the pelvic organs. Unless a complete diagnosis is made we have no knowledge of the pathological conditions prevailing, nor have we a syndrome sufficiently precise to

differentiate the case under treatment. Often it happens that in spasmodic dysmenorrhœa the first period after the beginning of a course of diathermy is free from pain. A patient has told me that this first period after the diathermy is the first one free from pain that she has ever had. Relapse, however, invariably occurs, and in attempting to combat this relapse on leaving off treatment, I have continued diathermy for over a year and have found that the pain gradually returns until the periods are just as painful at the end of that time as they were at the beginning.

The symptoms of painful menstruation dependent on an inflamed pelvic organ disappear, as does the inflammation, after treatment by intrapelvic diathermy, and the subsequent history shows that the patient remains well. This investigation of dysmenorrhœa shows the importance of diagnosis and of the following-up of cases. If the postulates just enumerated had been satisfied some claims that we have heard about the results of treating dysmenorrhœa would not have been made.

There have been two epoch-making events in modern electrotherapy. One is the production of instruments for measuring direct current, and the other the introduction of the diathermy machine.

Before the advent of the first, the work carried out could not satisfy the last of the postulates with the possible exception of that done with faradic currents.

In or about the year 1880, a handy instrument for measuring direct current first became generally available. The first observer to measure adequately the current he used was Dr. Georges Apostoli, of Paris. In 1886 he published the results of five years' work on the treatment of fibroid tumours of the uterus by direct current applications. He based his treatment on observations of the polar effects of direct current applied to dead tissues. It was observed that—using platinum or carbon as the active electrode—when it was the anode, the tissues in the neighbourhood of the electrode became dry and shrunken and acid in reaction: but when it was the cathode the tissue became moist and alkaline in reaction. In this latter case evolution of hydrogen disintegrated the tissue close to the electrode. Applying these facts to treatment in gynæcology, he found that a diminution in the size of fibroids took place, that the hæmorrhage was reduced in amount, and that the general condition of the patient improved. His cases were diagnosed, the progress of the case was properly recorded and followed up, the currents used were measured and there was a reasonable invariability in his results. The postulates were therefore satisfied. Although the claims which Apostoli made were accurate enough, the method fell into disuse as a means of treating fibroids, because the progress in antiseptic surgery provided a more rapid and effectual means of treatment. For a time it also fell into disrepute on account of the extravagant claims made for it by other less scrupulous practitioners. It remains, however, an effectual means of treating certain infections of the cervix.

The other epoch in modern electro-therapeutics was marked by the introduction of the diathermy machine. It came to this country three or four years before the Great War. The late Dr. Lewis Jones introduced it in St. Bartholomew's Hospital in 1910 or thereabouts for the purpose of removing new growths by coagulation. He does not seem to have developed its use for medical purposes. That it is useful in the hands of the surgeon is amply demonstrated, and it is becoming progressively established. However, I do not propose to speak about its employment in surgery, but to consider its uses for medical purposes.

The therapeutic use of diathermy has been standardized and kept within certain limits largely by the institution of a Diploma in Radiology and Electrology at Cambridge, and later at other universities. The examination of candidates for a diploma such as this necessarily establishes and maintains orthodoxy. This has been greatly aided by the teaching of Dr. E. P. Cumberbatch, former President of this Section, and by his standard work on the subject.

I shall divide diathermy treatment given for medical purposes into two classes.

Of one class, namely, that in which heating of more or less superficial structures to an indefinite temperature, or general heating of the blood to an unknown amount occurs, I shall say little. And here I am referring to treatment applied by two electrodes placed on the body or limbs, or by one electrode applied to the patient on a condenser couch. That is to say I refer to such treatments as are applied for the relief of pain, perhaps in the hope that some inflammatory state may be resolved, or for relief of certain cardiovascular conditions. There is no doubt about the utility of diathermy thus applied, and doubtless most diathermy treatments are given for one of these objects. But it is to this class of treatment that my remark especially applies regarding the lack of that clinical observation by which the postulates are satisfied.

I draw a marked distinction between this class and that in which an infected organ is heated to a certain critical temperature. I refer to the applications for removal of gonococcal infection of the cervix and urethra in women and its consequent effect on arthritis, for intrapelvic inflammations in women, for infected prostate in men and its effect on arthritis, and for puerperal fever.

In all these instances a special arrangement of the electrodes is used. Because diathermy currents tend to spread from the edges of electrodes and to take a superficial course, the intrapelvic organs cannot be heated by electrodes placed front and back or on each side. To procure this result one electrode must be more or less in the centre of a circle formed by the other.

*Puerperal Septicæmia.*—I will now describe 21 cases of puerperal septicæmia treated by diathermy at the West Middlesex Hospital.[1]

The method of application is by means of a vaginal electrode and lead belt as used for intrapelvic heating for inflammations of the pelvic contents.

| Total cases | Recovery after abscess formation | Recovery by lysis | Recovery by crisis | Deaths |
|---|---|---|---|---|
| 21 | 6 | 8 | 4 | 3 |

The above is a table summarizing the results in the twenty-one cases treated. Of the three patients who died one was moribund after six weeks' fever before treatment by diathermy was begun. She died after two treatments. Although the case was hopeless, treatment was carried out in order that it could not be said that any case was refused on account of its severity. One of the deaths occurred from septicæmia following abortion. All the other cases were after full-time confinement. It may be that there was some element present in this case which was absent in the others.

The third death occurred two days after the temperature had fallen by crisis. The cause of death was pulmonary embolism.

The patients who formed the subject of this investigation were all very ill. There can be no doubt that without the intervention of diathermy most of them would have died.

One thing we have learnt is that cases of sapræmia must not be treated by diathermy. Patients with sapræmia are suffering from absorption of toxins from a putrefying mass in the uterine cavity, physiologically outside the body. To heat that is only to increase the amount of poison formed and increase the toxæmia.

Chart I is that of the first case treated. There was an initial rise of temperature due to sapræmia, but, as a result of intra-uterine douches and glycerine injections, the temperature fell. It rose again, however, as a result of septicæmia and abscess formation. Diathermy was given towards the end of the second week of illness, and was followed by a fall of temperature to below normal. It rose again, and, four days later, diathermy was again given. This was again followed by a fall to normal. Again the temperature rose and diathermy was given more frequently.

[1] That the work has been done there is due to the sympathetic interest and kind coöperation of Dr. J. B. Cook, the Medical Superintendent.

Temperature continued to rise, due to abscess formation. After the abscess had been opened the temperature fell and remained below normal. The patient made an uninterrupted recovery from this point.

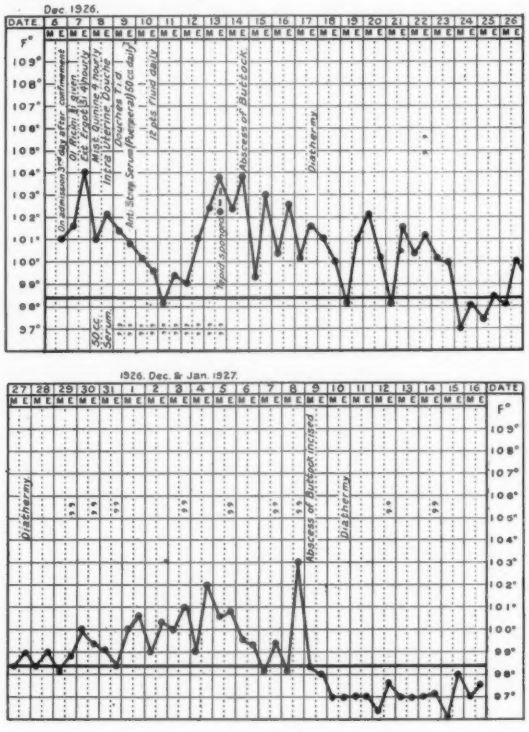



CHART I.

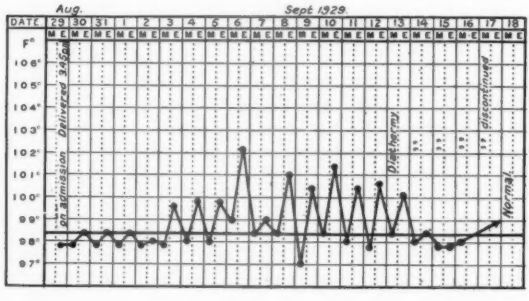



CHART II.

Chart II is that of the last patient to be treated by this means. She had a breech presentation and had been considerably mishandled before admission to hospital. On admission she was still undelivered, and the posterior vaginal wall was extensively

torn. The cervix was lacerated and the perineum was ruptured. In spite of all endeavours to prevent infection through the lacerations septicæmia developed. About ten days after the onset of fever diathermy was begun. At that time evening temperature was from 100° to 101° F., with morning remission. After the evening of the day on which diathermy was first given the temperature did not rise again and the patient made an uneventful recovery.

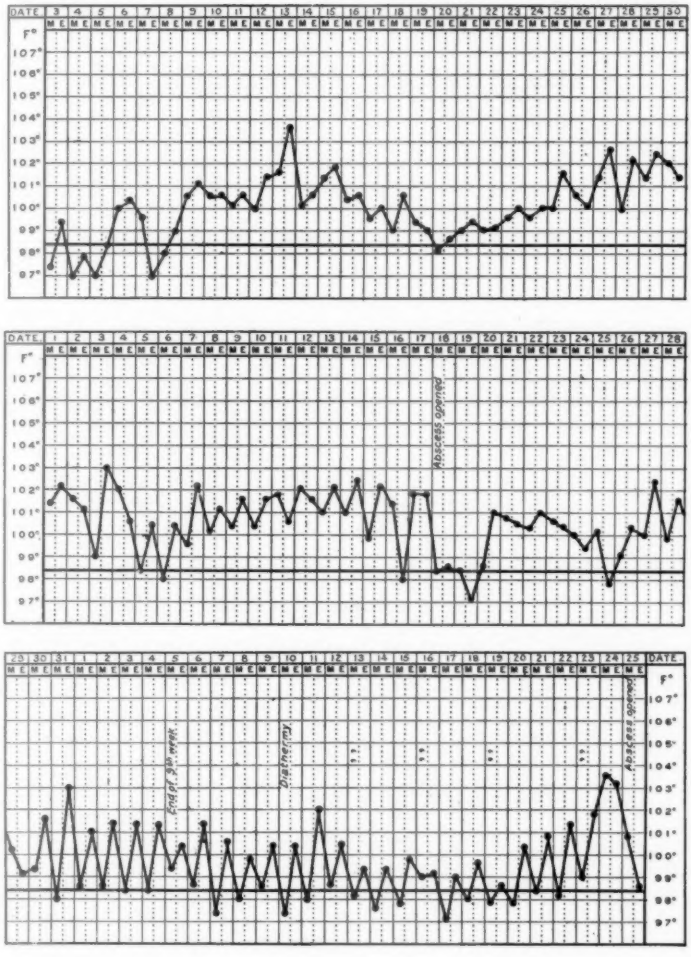



CHART III.

Six patients recovered after abscess formation, and of this group Chart III may be taken as representative. After about seven weeks of fever an abscess was opened and the operation was followed by normal temperature for two days. The temperature then rose again, and at the tenth week of illness, diathermy was

applied. This was followed by a fall of temperature, but not quite to normal, and there was a subsequent rise, due to a further abscess formation. After the abscess was opened the patient rapidly recovered.

Eight patients have recovered by lysis. Of these the case recorded on Chart IV may be taken as an example. In most of the cases, as is well shown in this one, there is a fall of the initial fever temperature to normal following the relief of sapræmia by intra-uterine douches and glycerine injections. Diathermy was begun in the middle of the fourth week of illness, and in five or six days' time the patient was convalescent.

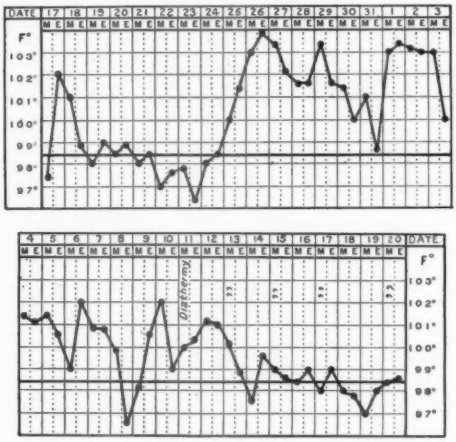



CHART IV.

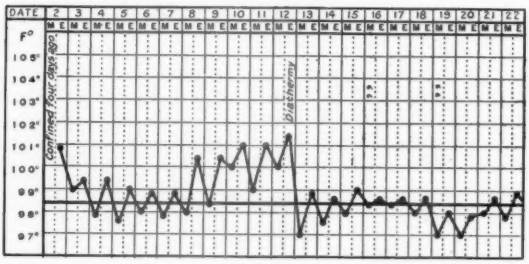



CHART V.

The fever ended by crisis in four cases, or in five, if the case in which death occurred two days after crisis from pulmonary embolism is included. This class is represented by Chart V.

Accounts of the special technique for treating gonococcal infections of the cervix and urethra in women, and of the results of the treatment, have been repeatedly published. The abolition of the infection fails in about that proportion of cases in which reinfection would be expected to occur. As a matter of fact the successes —established as such and followed up—amount to over 90%. In other words, the

result is invariable. In cervicitis, not due to gonorrhœa, the successes are about 80%.

In the electrical department of St. Bartholomew's Hospital, out of 19 cases of arthritis in which cervical infection, gonococcal or otherwise, was found, treated, and followed up, 6 ended in complete success, 9 were improved up to a point and 4 ended in definite failure. In the 9 "improved up to a point," the inflammation of the joints subsided, but complete functional restoration of the joint was not obtained on account of the damage done. These cases are successes in that the inflammation was brought to an end. As far as the effect on the inflammation is concerned there were 15 successes out of nineteen cases.

A paper on the technique and results of treating pelvic inflammations in women by diathermy was read before this Section in December, 1928.[1] Here, again, the results are invariable when allowance is made for imperfections in diagnosis and for some special difficulties in carrying out the treatment in some of the cases. Roughly 80% of these cases were successful. The claims made for the results of treating prostates and vesicles infected with gonorrhœa, by this method, appear to have been misunderstood. Treatment of a prostate and vesicles infected with gonococci invariably has a marked effect upon metastases resulting from the infection. I have carried out this method of treating prostatitis for gonorrhœal arthritis for the last eight years, and say quite positively that subsidence of inflammation of joints invariably occurs as a result. The ultimate range of movement and amount of usefulness obtained depend on the amount of damage sustained before treatment begins. Other metastases resulting from gonococcal infection of the prostate and gonococcal septicæmia are, so far as I know, as invariably cleared up as is the arthritis. But when it comes to claiming that the prostate can be cleared of infection by this means, there is not the same certainty. I, at all events, have never made this claim. In some cases it may be so, but the results are not in the same category as those obtained by the treatment of the cervix and urethra in women. It is not safe, perhaps not possible, to heat the whole infected prostate and vesicles to as high a temperature as that to which the whole infected area in the cervix and urethra in women can be heated. Moreover, the certainty of knowing whether a cure has occurred is not so great. In the case of the cervix and urethra, the relief of symptoms and return to normal appearances, observed over long periods, make the diagnosis of freedom from infection a reasonable certainty. The same observation of the prostate and vesicles is not possible, and negative results of microscopic examination of smears after prostatic massage are of little value. But, I repeat, the effect on the metastases is invariable.

This work on heating infected organs by diathermy satisfies the postulates. The cases are diagnosed and the pathological condition is known with sufficient accuracy to enable them to be properly classified. Notes on the progress are kept and observable physical conditions are recorded. Results have an invariability which is sufficient. These cases have been followed up, in spite of the difficulties of doing so, in many cases for two or three years.

In describing the results I have used the word "invariable." All I mean by that is that they can be repeated with a constancy sufficient to establish the relationship of cause and effect. The failures are not more than would be accounted for by errors of diagnosis, special difficulties of application in certain cases, and reinfections. The current applications have been measured.

*Pneumonia.*—Owing to the progressiveness of Dr. J. B. Cook, the Medical Superintendent, and to his coöperation, up to the present time 89 cases of lobar pneumonia have been treated by diathermy at the West Middlesex Hospital, and complete records of these are available.

[1] C. A. Robinson: "Treatment of Pelvic Inflammations by Diathermy," *Proc. Roy. Soc. Med.*, 1929, xxii (Sect. Electro-Therap.).

This was, I believe, the first hospital in this country at which pneumonia was treated by diathermy. At all events, so far as I know, it was here that the treatment was first systematically carried out, and it has the greatest number so treated to its credit. These cases have been chiefly under the immediate charge of Dr. Marjory Warren, and it is owing to her zeal that the notes of the cases have been so complete.

Speaking generally the results have been relief of pain, a tendency to rest and sleep, less necessity for sedatives, and a general improvement in the condition of the patients. This is almost universal, but, it cannot be claimed that a really sleepless or delirious patient has the distressing symptoms removed, possibly owing to the difficulties of application in such cases.

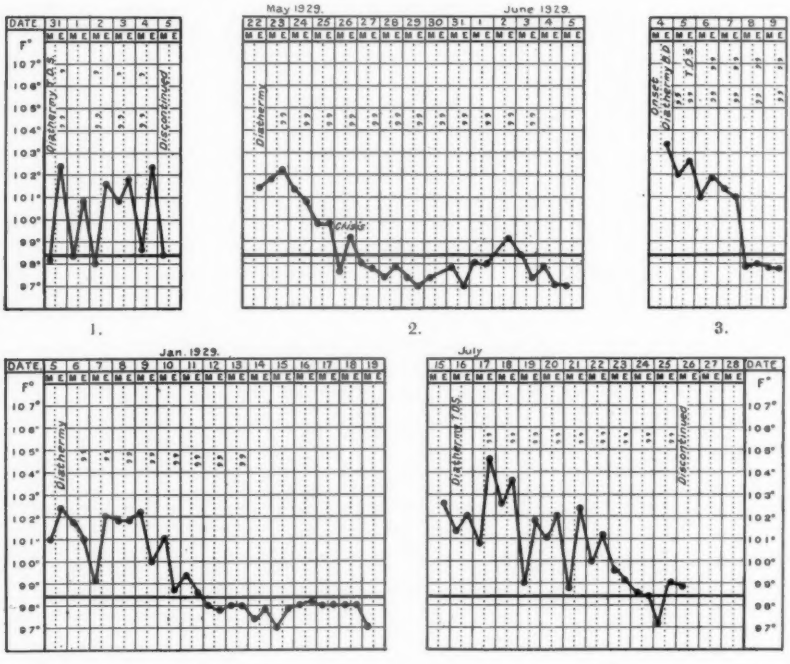



CHART VI.

There is no doubt about the benefit obtained, and this is probably reflected in a lowering of the death rate, though this is difficult to prove. Ten deaths have occurred in the 89 cases. During the period over which the investigation has lasted, we have passed through several severe epidemics. The patients were suffering in many instances from the effects of starvation and exposure, and were in bad condition. The number of deaths (10) must be considered low. Whether diathermy treatment or the general care and good nursing which these cases have had is responsible is another matter.

That the method is considered to be useful is shown by the fact that, beginning with a ward of three beds for men, Dr. Cook has had the facilities for the treatment extended to include that of women, and we now have one of the large wards provided

with diathermy for the treatment of men. A team of sister and nurses, especially trained in the application, is employed. The method consists of placing a metal electrode (1 lb. lead) 6 inches by 8 inches, back and front, with as little disturbance as possible. The current is increased up to tolerance, and is given for 20 minutes every four hours during the day. In these cases I have sought evidence to show whether there is a specific reaction to the treatment. Crisis occurs early in so many cases treated by the usual methods and the date of onset is often so difficult to determine that no claim can be made that crisis occurs earlier on account of the treatment. On the whole I believe that the duration of the illness is not shortened.

Specimen temperature charts to illustrate the classification are shown above. In the first, no effect on the temperature has been produced, and this is classified as "ending by crisis unaffected by diathermy."

In the second and third there is a fall of temperature between the beginning of diathermy treatment and the crisis. Such cases are classified as "ending by crisis and possibly affected by diathermy." In the fourth ending is by lysis. There is no reduction of temperature for four days following the commencement of diathermy treatment. These are classed as "ending by lysis, unaffected by diathermy."

In the fifth, there is ending by lysis, fall of temperature commencing shortly after the beginning of the treatment. These are classified as "ending by lysis, possibly affected by diathermy."

TABLE OF RESULTS (89 CASES).

| | Classified 74 cases | | | Unclassified 15 | |
|---|---|---|---|---|---|
| | Affected by diathermy | Unaffected by diathermy | Total | | |
| Ending by lysis | 17 | 5 | 22 | Irregular | 9 |
| ,, crisis | 9 | 33 | 42 | Empyema | 6 |
| Deaths | — | 10 | 10 | | |
| Total | 26 | 48 | 74 | | |

In 42 of the 74 classified the illness ended by crisis. In 33 of these the general course of the fever was unaffected by the diathermy; that is to say there was little or no lowering of the temperature between the time of first giving diathermy and the crisis. In 9 there was a lowering of the temperature during this time. Twenty-two of the classified cases ended by lysis. In 5 the temperature remained at the same level for some days after diathermy was first given and then began to fall. There were therefore 17 cases of lysis which may have been affected by the diathermy. In these cases ending by lysis a patient has frequently become quite suddenly well, as if crisis had occurred when the temperature at the time was only 99° F.

In 9 cases the ending was irregular, or for some reason the case was not capable of classification. Six cases ended by empyema. Adding the 9 cases of crisis in which a distinct lowering of the temperature after diathermy had occurred to the 17 cases of lysis which may have been due to the effects of diathermy, we have 26 cases affected by it, and adding the number of deaths (10) to that of those cases of crisis unaffected (33), and lysis unaffected (5), we have 48 unaffected out of 74 classified.

In this treatment of pneumonia by diathermy, so far as the specific effects of heating an infected organ are concerned, the postulates are not satisfied. The current applications to the infected areas are not known with sufficient accuracy and the results are variable within the meaning of the postulates. We are trying to heat an infected organ to a certain critical temperature by electrodes, both of which are placed on the surface. The method is the same as that employed when we aim at relief of pain, or relief of symptoms, or perhaps at resolution of inflammatory products, by means of diathermy, applied in such a way that structures heated and

temperature reached are not known with any degree of accuracy. We are using here a method which does not sufficiently mitigate the effect of the tendency to spread—which is characteristic of diathermy currents—as might be done by placing one electrode within the circle formed by the other. When this can be done and a certain definite temperature can be reached, definite results are obtained, invariably constant within the limits of errors of diagnosis, failure due to extraneous events—such as reinfection, imperfections of applications and consequent inadequate heating and peculiarities of the patient, such as inability to respond. In this treatment of pneumonia the area of consolidated lung will not always be heated by the current and probably never heated throughout its entire extent. This accounts, at least in part, for the limitation of the results obtained and for their variability. I believe that if we could arrive at a technique by which we could, for instance, heat an infected lung as certainly and as completely as we can heat an infected cervix, we should obtain the same uniformity in results.

This does not mean that the method is not useful. It means that the evidence of specific effects of heating the infected organs is unsatisfactory.

We have a great variety of instruments enabling us to produce muscular contractions, changes in blood-supply, and polar effects near the electrodes, as well as heating deeply and, especially, to heat certain organs. A knowledge of the physical, chemical and physiological effects of the applications is helpful but not essential, because most of the treatments are empirical. What is required is investigation on the lines of what may be called intelligent empiricism. As has happened in other branches of therapeutics, the most striking and important results have often been obtained by empirical observation and we may do much by a simple method of trial, provided the postulates are satisfied.

*Discussion.*—Dr. G. SIMON referred to the results in seventeen cases of lobar pneumonia treated by diathermy at Saint Bartholomew's Hospital; as shown by the charts, the level of the temperature, pulse and respiration, between admission and the occurrence of crisis or lysis, was unchanged in the majority of cases, and neither in these respects, nor in the white blood-count curves was there any evidence of a specific response.

Three patients had died and the post-mortem findings showed no evidence that diathermy had had any local effects on the lung. The relief of pain had been considerable, and on the occasions when all other means, including antiphlogistine, leeches and omnopon had failed, diathermy had afforded great relief.

Mr. MARTIN OLDERSHAW said that it was very difficult to give a prognosis in cases of puerperal sepsis. In apparently mild cases the patient might die, and in an almost hopeless case she would sometimes recover. Any addition to the means of treatment was therefore welcomed. Dr. Robinson had drawn sharp distinction between sapræmia—in which, he said, diathermy was of little use—and septicæmia, in which he had found it of great value. Clinically, however, patients could not be readily classified, and many—perhaps most cases—were of a mixed type. He (the speaker) assumed that whenever there was a clear evidence of putrid material inside the uterus, this should be removed before diathermy was applied.

In puerperal infection, as indeed also in pneumonia, the real problem was to raise the patient's general powers of resistance. Apparently diathermy could help in this respect, partly by its local heating action on the infected organ, and also by relieving pain and promoting a feeling of general well-being.

Dr. G. B. BATTEN said he remembered that about 26 years ago Dr. Lewis Jones (of beloved memory) had drawn the attention of the British Electrotherapeutic Society to two features in our special work: the relieving of symptoms and the—more important—curing of disease or its consequences, as of the disabilities after paralysis, or of sciatica. He (the speaker) felt sure that Dr. Lewis Jones would have considered Dr. Robinson's results even more important.

# Section of Obstetrics and Gynæcology.

President—Dr. ARTHUR E. GILES.

[*November* 15, 1929.]

## A Patient who was Operated on in 1914 for Neo-natal Subdural Hæmorrhage.

By CLIFFORD WHITE, F.R.C.S.

THIS patient was asked to attend this meeting for examination because cases operated on at birth for subdural hæmorrhages and followed up for fifteen years are uncommon.

This boy was delivered on August 2, 1914, at Queen Charlotte's Hospital. The mother had a contracted pelvis and the forceps was used. On delivery, there was a large depressed fracture in the left frontal region; the heart was beating well and respiratory movement was present. I saw the child within an hour of delivery, when he was still quite unconscious. I turned down a large skin flap round the depressed fracture, and then a flap of the skull corresponding to the area of the depressed fracture. Underneath the dura mater dark blood could be seen; the dura was therefore freely opened and about an ounce and a half of blood-clot evacuated. I replaced the dura and put in a small gauze drain under the scalp for two days. The child made an uninterrupted recovery. I saw him again a month later and he was doing well. There was no history of convulsions.

Owing to the accident that the mother happened to come to my Out-patient Department at the Samaritan Hospital with prolapse, and attended regularly for years, I had the opportunity of following the progress of the child.

I have a note that on May 10, 1915, he was crawling and able to speak a few words. In October, 1916, he was talking and walking well. In May, 1918, his intelligence and general development seemed in every way equal to that of any child aged 4. In October, 1920, there is another note to the same effect.

Those who have examined him this evening will agree that he is now a rather heavily built lad for 15 years of age. His thick hair covers the scar in his scalp. His health is good, and his intelligence perhaps rather above the average, as he passed out of his school some months ago and is now at work and earning money.

I think it is important to recognize that a child who has had a subdural hæmorrhage efficiently evacuated may become a normal individual and an asset to the country, whereas simply levering up the depressed bone and not even investigating the condition of affairs beneath the dura mater merely achieves a cosmetic success and does not treat the essential lesion, or prevent subsequent nervous disease or mental defect.

This is the only case that I have been able to follow up after operation, but I have brief notes of two other cases in which a large skull flap was turned down and the dura mater inspected to see if a subdural hæmorrhage was present. In both cases the child recovered from the operation, and therefore it would seem that the mortality is not unduly high, and there is no reason why radical treatment should not be adopted in these cases.

## A Case of Tuberculosis of the Canal of the Cervix.

By CLIFFORD WHITE, F.R.C.S.

MRS. H. T., aged 64, came to the Samaritan Hospital on May 31, 1929, complaining of blood-stained vaginal discharge of three months' duration, also of backache of the same duration, and rapidly increasing weakness. The ovaries had been removed on account of menorrhagia thirty years previously, and there had been no menstruation since. She had had two children and three miscarriages. There was no abdominal pain and there were no urinary symptoms. She was seen in the Out-patient Department by Mr. Leslie Williams, who removed a small piece from the portio vaginalis for microscopic examination. The section was not very satisfactory, and the patient was admitted under my care on June 17, 1929.

She was extremely thin, but no abnormal physical signs were noted in heart or lungs. The abdomen was not distended. There was no free fluid, and no abnormal mass could be palpated. On examination *per vaginam*, the body of the uterus was not found to be enlarged, and there was no tumour in either of the fornices. The cervix was rather hard, no definite outgrowth present on the portio vaginalis, but blood was oozing from the external os. There was no thickening in the broad ligaments. On rectal examination, the utero-sacral folds were found not to be thickened.

Two days later, under anæsthesia, I scraped away what I took to be a malignant area around the external os and inserted nine needles containing a total of 49 mgm. of radium. These were left *in situ* for seventy hours.

The portion that I scraped away consisted, as I now know, of granulation tissue, but when I saw the section I believed it to be a portion of a sarcoma. I therefore thought the uterus should be removed and performed a total hysterectomy July 3, 1929. The operation was very difficult, owing to the dense adhesions in the pelvis. Whether these resulted from the oöphorectomy of thirty years ago, or were due to the radium, I cannot say. There were no signs of tuberculous disease noted anywhere in the abdomen.

About a week after the hysterectomy an offensive vaginal discharge was reported, and this soon became fæcal, owing to a recto-vaginal fistula high up in the vagina. It was thought probable that this was the result of the radium.

The patient's weakness increased and she did not respond to treatment. There was no cough or other symptom to point to any definite complication, but she died July 24, 1929, three weeks from the time of operation and five weeks from the insertion of the radium. No post-mortem examination was obtained.

The uterus, after hardening, measures 6·5 cm. long, 5 cm. broad, and 2·5 cm. thick. The wall and cavity of the body of the uterus appear to be normal. The endometrium is not thickened or ulcerated anywhere. The external os is rough, dark red in colour, and covered by granulation tissue. The canal of the cervix is expanded into a caseous mass 1·7 cm. long and 1·3 cm. across at its widest part.

Sections taken through this area show numerous giant cells—of the type usually found in tuberculous foci—as well as caseous tissue. In the wall of the cervix at the edge of this caseous area there are several typical tubercles, leaving no possible doubt as to the tuberculous nature of the cervical lesion. A section of the endometrium shows no tubercle.

As far as my investigation of the rest of the abdomen went, no other tuberculous focus was present, and, as already stated, there were no signs of active phthisis. Hence it would appear that this is a case of primary tuberculosis of the cervical canal.

# Maternal Mortality and its Relation to the Shape of the Female Pelvis.

By KATHLEEN VAUGHAN, M.B.

ABSTRACT.—Both in the modern and the ancient world, among women who are out-of-door workers and among those who live in natural and primitive conditions, childbirth is easy and safe.

The inlet of the female pelvis approaches a circle. The circular form of inlet allows a larger fœtal head to pass than the same measure disposed in any other form.

In the circular pelvis the sacro-iliac joints are well developed by constant use and are freely movable.

In contrast to this, civilization with its confinement of children indoors, and its absence of sunlight on the skin necessary for the proper calcification of growing bone, and the disuse of the sacro-iliac joints, alters the normal shape of the pelvis and makes childbirth difficult and dangerous. This change in pelvic shape leads to an undue proportion of undersized children surviving the ordeal of birth as the children with the larger heads who would easily pass the circular inlet are born dead.

The last report on infant mortality tells us that two-thirds of all the stillbirths and infant deaths are due to prematurity and obstetric trauma, and the *New Statistical Review* issued in 1927 tells us that 20% more of the stillbirths are males.

The natural proportion of males to females is thus upset, only the smaller children are born alive, hence perhaps the eventual decay of all civilizations, past and present.

I venture to suggest that the solution of our maternal mortality problem does not consist so much in elaborate provision for abnormal childbirth as in trying to regain the lost heritage of natural and easy birth. We must begin with the newborn female child and her development, and return to nature as regards light, food and exercise, and thus we shall ensure proper development of the pelvis so that childbirth becomes again easy and safe.

THE statement by the Ministry of Health that in spite of more ante-natal care and better midwifery, the maternal mortality rate in England and Wales shows no improvement on the returns made twenty years ago, makes one think we have not got to the bottom of the problem. Maternity, for some reason, becomes more and more dangerous for the mother, and some factor is at work which is evidently untouched by the provision of skilled obstetricians and midwives. I venture to suggest that it is civilization itself that is at fault, and that is bringing itself to an end by creating conditions of life that so deform the pelvis of the race that the woman's pelvis is no longer capable of allowing the child's head to pass without risk to the mother and perhaps death to the child. Those that are safely born are the premature, the children with smaller heads, and consequently, the females, who have a better chance of surviving the ordeal of birth.

I began to study the problem in Kashmir, where Cæsarean sections are as common as they seem to be in China. The women with contracted pelves all come from the better and more civilized classes, who, owing to social custom, are imprisoned with little light and without the food factors necessary to compensate for this deficiency—hence imperfect calcification of their bones leading to gross changes in the skeletal anatomy. I noted that in the same town the boat-women living in the open air, with but one garment, engaged in heavy work with the men, eating a coarse but sufficient diet, consisting of milk, eggs, cheese, rice, mustard oil and abundance of raw fruit and vegetables, had their children with no trouble and never came to hospital on account of difficult labour.

All over India the upper-class women, e.g., those living in seclusion and known as "purdah women," are the ones who have obstetric complications, whilst the field workers, such as the tea-garden coolies, women working in rice fields, knee deep in water, women who cut grass for the horses, the boat-women and the

women of nomadic tribes, such as live on the North-West Frontier in tents—these have their children with hardly any trouble, and therefore no skilled attendance at birth is needed. Furthermore, the very women who, when living in natural open-air conditions have easy and natural confinements, when transplanted to the city, or shut up in "purdah," have difficult and dangerous ones with their younger children. Outside Bombay the weaver-caste women living in their own villages, tending cattle, and engaged in the ordinary tasks, such as drawing water, fetching wood, preparing the usual cow-dung cakes for fuel, and other tasks which fall to their lot, have no trouble in parturition and have large families, but when brought into the city and obliged to live in narrow dark streets on the ground floor behind the husband's loom, they become deformed, and the Cama Hospital for Women in Bombay reports that were it not for the constant influx of fresh workers from the country, this caste would die out. In China, Maxwell, Miles and Feng report that their Cæsarean cases occur chiefly among those women who bind the feet (the superior class of Chinese), who live much indoors and are incapable of taking any exercise. Many travellers have described the African negress living in her kraal, going out daily to her work of tending cattle, etc. She has her child in a few minutes and takes it up in her arms at birth and goes on with her work, but skilled observation of the negress living in New York, or in any of America's big cities, reveals another state of things. Whitridge Williams, of Baltimore, says: "Were it not for the greater compressibility of the negro infant's head there would be more Cæsarean sections needed among them for deformed pelvis than among any other class of the community." He also says: "The fact that the usual types of contracted pelvis occur four or five times more frequently in coloured women, renders it highly probable that the explanation of the difference must be sought in certain conditions peculiar to that race, and, from the study of coloured woman as seen in my service, these would appear to consist in imperfect general development and rachitis which may be regarded as resulting from the imperfect nutrition and poor hygienic conditions under which the coloured women live in large cities."

Nearer home, the Carnegie Trust Report, 1917, gives interesting examples of islands such as Shetland and Skye where the women, until recently, were delivered without midwife or doctor and had large families of healthy children—nine, ten, twelve or more were not uncommon—and they did not die in childbirth—yet those women were working barefoot with the men, hauling in the nets and the boats, and doing laborious field work such as drawing the plough while the men guided it. The same report notes that in crowded areas and towns in Scotland, notably Glasgow, the women have rickets and every possible obstetric complication, and the maternal mortality is very high.

In England and Wales Dr. Janet Campbell's report on maternal mortality, 1927, tells us that we lose over two thousand five hundred mothers annually in childbirth. The highest rates I note are in industrial centres, smoky cities and overcrowded towns.

Thus evidence from all over the world indicates that a natural life with hard work and exercise in the open air is good for women and ensures natural, easy, and safe labour, whilst civilization with its crowded cities, indoor life at school and at home, exclusion of sunlight and air, and the impossibility of obtaining fresh and natural food, produces new and dangerous complications for both the mothers and the infants of the race.

The fundamental cause of difficulty is obvious—that for some reason the child's head and the mother's pelvis do not fit, and delayed and difficult labour is the result; bruising of soft parts, exhaustion of the mother, the risk of sepsis, all follow on this primary failure of adaptation.

Which is at fault? Is the fœtal head too big, or the maternal pelvis too small?

Fitzgibbon says that in 75 per cent. of all cases of medium and of contracted pelvis the women will deliver themselves if time is given, and Whitridge Williams gives it as his opinion, in America, that, "provided the pelvis is normal, it is unusual for children weighing less than 11 lb. to cause difficult labour, simply from their size." In India, Holditch Leicester and Lane traced a relationship between the racial head and the capacity of the racial female pelvis, showing that the size of the child's head was proportional to the mother's pelvis and that both varied in size according to the race to which they belonged.

Verneau, in 1875, published an exhaustive monograph on variations of the pelvic shape as regards both sex and race, but he found, like our obstetricians of to-day, that the female pelvis was subject to such extreme variations in shape, even in the same race, that in the end he confined his observations almost entirely to the male pelvis of the different races of mankind. Our Western text-books also are by no means of one mind as to what are normal pelvic measurements.

By the kindness of Sir Arthur Keith I was enabled to measure some pelves at the Royal College of Surgeons.[1] To measure the inlet of the pelvis I used a piece of string, carrying it along the ilio-pectineal lines, across the inner side of the pubes and across the sacrum just below the promontory. After all, it is the *capacity* of the pelvis that matters, and I tried to get an idea of this by pinning out the measuring string on paper. It was obvious that, arranged as a circle, it contained a larger area than when it was arranged in any other form, and that the least deviation from the circle diminished the available space for the child's head.

Therefore the capacity of the pelvic inlet depends more upon its shape than its size.

I then studied the variations in shape in a number of female pelves in different races, and measured the transverse and antero-posterior diameters of the brim to get an idea of the variation from the perfectly circular form. The European, Englishwoman, Frenchwoman, Russian and Egyptian pelves were flattened from before backwards, having the longest diameter transverse. Then I came upon some pelves whose inlet approached the circle, and finally the Andaman Island female specimens 1216, 1212, 1213, the Sikh woman 631 B, Peruvian f. 1013, S. Australian f. 1068.15, and Negress No. 1256.51 whose transverse and antero-posterior diameters are of equal length, and consequently the pelvic inlet or brim is a perfect circle.

I also examined some innominate bones, notably one from Ur of the Chaldees, one from Salisbury Plain (Ancient British) and an Anglo-Saxon specimen where the great roundness of the ilio-pectineal line is marked, and was led to the conclusion that the more untouched by civilization and modern habits of life, the more clearly circular the pelvis. All these people must have borne their children in primitive conditions without doctor or skilled midwife.

Can there be any racial cause for these differences in form? I think not, for it was at once apparent that the round-headed race, such as the European, is born of the oblong pelvis, and the long-headed race, such as the Bushman, of the round pelvis, so that the shape of the female pelvis does not vary to accommodate the varying shapes of the head in the human race.

Again, the fœtal head is circular and is made to mould into a perfect circle by means of three sutures, and a larger fœtal head can be born through a circular inlet than through any other form of inlet having the same boundary measure.

To illustrate this we have only to think of a cup and ball; any slight deviation from the circular in the cup will prevent the ball entering.

Lynch conclusively proved by X-ray studies that the pelvic inlet stretched at the three pelvic joints. His studies are also interesting as showing that the ends of the oval pelvis are not occupied by the child's head as it passes through.

I found there were two types of female pelvis amongst those I had measured.

[1] Also owing to the kindness of Sir Arthur Keith the paper was illustrated by the specimens indicated.

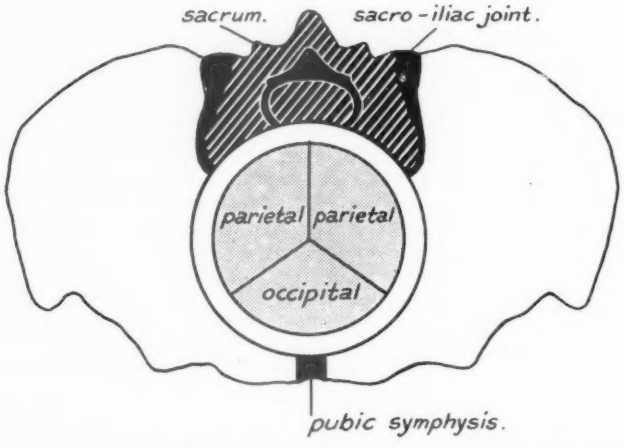
(1) The perfectly circular, in which the whole of the body of the first sacral vertebra is outside the inlet.

(2) The transversely contracted or rickety, in which not only the upper part of the sacrum falls forwards and downwards and bulges into the cavity, but there is also a descent of the fourth and fifth lumbar vertebræ with it—all helping to block up the available space.

If there is the slightest departure from the circular form, trouble follows with the fœtal head, because the area available for its accommodation is lessened.

Again, in the European pelvis the head descends, during birth, in a screw-like manner, because the three largest diameters of the pelvis are in different pelvic planes.

In the round pelvis all is simple, quick, easy and safe, and it will accommodate the largest head which the circumference can enclose. All the diameters in all the three planes are equal (or speedily become so in labour) with movable sacro-iliac joints. The sacrum swings back as on hinges, the ilio-sacral ligaments are flexible and elastic as in the perineum, the head is kept to the front by the posture of the mother (squatting), and birth is rapid and easy.




Fœtal head in maternal pelvis. Looked at from above as if head were transparent. To show how the lines of compression in the skull alternate with the lines of expansion in the pelvis. Note how sacrum forms part of the circumference of the inlet.

*Native Midwifery.*—The woman constantly uses the squatting posture, and this no doubt keeps the child's back against the mother's abdominal wall; there is no trouble with the perineum, as it is daily stretched in this position, its muscles are exercised and strong, and it remains elastic. In natural delivery, as practised among people who have primitive traditions regarding childbirth, I have seen the woman have her child in the kneeling posture with knees apart and leaning backwards, held up under the armpits by mother or friend who kneels on the ground behind her, so that the child is literally born on the helper's knees, as, we read, Bilhah's child was born on Rachel's knees (Gen. xxx, 3). The patient then lies down, and shortly after gets up into a kneeling position once more, presses her abdomen with both hands and the placenta comes away.

Of course, things are not always so simple. In Kashmir, if there is any difficulty, the native midwife places the patient on her back, flexes the legs on the thighs and

the thighs on the abdomen, rotating them outwards so strongly that the abdomen occupies the space between them. This position lifts the front of the pelvis which swings upwards on the sacro-iliac joints and gives the already engaged head more room. Another posture they use is the squatting, as if for defæcation, and again the crouching or kneeling position with the body bent. These traditional manœuvres are the result of ages of experience that the pelvis is a movable ring, and that pushing the forepart up or down increases the capacity of the inlet, and stretches the articulations and the perineum. Greater increase in the conjugate is gained in the extreme thigh flexion attitude (such as can only be seen and practised in the East, where the sacro-iliac joints are in constant use), than by the Walcher position which depresses the pubes to a lower level than the sacral promontory.

*Sacro-iliac Joints.*—Duncan pointed out that pelvic development was influenced by the sacro-iliac joints, and we know that anchylosis of these joints produces atrophy of the sacrum and both ilia, and that where only one sacro-iliac joint is affected, the pelvis fails to develop only on the anchylosed side, and the earlier the anchylosis takes place the more complete is the deformity produced.

Whitridge Williams and Merkel have both testified to the rapid growth of the pelvis in girls just before puberty, and they draw attention to the fact that it chiefly affects the increase in width of the sacrum and that part of the os ilium extending from the sacro-iliac joint to the acetabulum—in fact all the parts near the sacro-iliac joints.

In handling the pelves at the College of Surgeons, I noticed how differently the sacro-iliac joints were developed.

The auricular surface of the sacrum extends over the first three sacral vertebræ, and this surface is much more extensive in native races, so that there is a larger surface covered with cartilage to influence bone growth. The second sacral vertebra has a depression into which a projection of the os ilium fits. This projection is situated at the junction of the upper two-thirds with the lower third of the articular surface, and it acts as a pivot on which the sacrum moves backwards and forwards, the range of movement being greater above this projection than below. We thus see how movement of the sacrum backwards, as it swings between these two pivots, brings the concave surface of the first sacral vertebra (the part just below the promontory) into line with the ilio-pectineal line and, in the circular pelvis, completes the circular form of the inlet. All circular pelves have this joint well developed: cf. Negress 1256.51, Fuegian f. 1252, S. Australian 1068.15, Ancient British f. pelvis found on Salisbury Plain 174·1, the pelvis from Ur of the Chaldees (College of Surgeons Museum). In all these the knob or boss on the auricular surface of the ilium was well marked and the auricular surface extensive.

Havelock Charles, in 1894, showed how the influence of function has modified the Punjabi sacro-iliac joints, producing a larger articular surface which, he says, is common to all Oriental races and is similar to those found in prehistoric man.

It seems to me that there should be in all men and women, as in Orientals, a mobility of this joint and a constant change of pelvic inclination as the subject walks, runs, sits, stands or crouches, and that the immobility of the joint leads to serious changes in the shape of the pelvis, and of its inclination.

The squatting posture used by both men and women while sitting, and also when attending to the calls of nature, was, of course, also employed by primitive man for the same purpose.

Observe now the habits of the Indian woman, of the Shetland woman, in fact, of all those who live natural lives and exercise their sacro-iliac joints, by hard manual labour: digging, weeding, hauling-in nets, carrying and lifting heavy weights, and—more important than all—the daily crouching posture for defæcation and urination. This posture is really the natural one and all these people are without the modern closet, and many are without chairs.

Amongst modern civilized peoples the sacro-iliac joints are never used except in games or gymnastics. Our chairs get higher and are made to avoid stooping—our agricultural implements the same. Our first care in educating the young is to teach them to "sit quiet," and they are made to sit up on their still soft and cartilaginous pelves for hours at a time, while we prevent them playing the games natural to them—crawling and rolling and crouching. They are taught to pass their motions in an utterly unnatural position sitting up with their legs dangling. Later on, heels on the shoes tilt the body forward and are compensated for by more curving of the spine in the lumbar region, or by tilting up the fore part of the pelvis and thus exposing the pelvic floor to increased strain.

At birth the pelvis is almost entirely of cartilage and the inlet circular in both boys and girls.

The two most rapid periods of pelvic growth are noted in girls, from birth till five or six; again, from eleven till fourteen or fifteen.

Confinement indoors with absence of light and poor food, in which vitamin D is deficient, initiates rickets in early life. Before and at puberty the same causes operate even more strongly, and long-continued sitting and an indoor life induce the changes we are accustomed to consider normal, and the kidney-shaped pelvis is the result, in which the space intended by nature to accommodate the fœtal head is diminished by one-third or even one-half.

## Discussion on the Report of the Departmental Committee on the Training and Employment of Midwives.

**Dr. Herbert Spencer**: The reference to the Committee was: "to consider the working of the Midwives Acts 1902 to 1926, with particular reference to the training of midwives (including its relation to the education of medical students in midwifery) and the conditions under which midwives are employed."

The Report is divided into five parts: (1) Historical survey, (2) maternal care, (3) training of midwives, (4) employment of midwives, (5) administration.

The Committee consisted of 12 members, of whom only one, Dr. Fairbairn, is an obstetrician.

The Report is signed by all the members, but with reservations by two members, Dr. Fairbairn and Mrs. Richmond, who dissociate themselves from the majority of the Committee in those recommendations that involve the splitting up of the functions hitherto assigned to the Midwives Board and their distribution between a reduced Board, the Ministry of Health and an advisory Committee (paras 100 to 194). They urge "that no such momentous changes as those recommended in this Report should be made without full and open discussion, not only with the midwives, teachers, teaching schools, and other interested parties in England, but also with the sister and similarly constituted Boards in Scotland and both divisions of Ireland, with which there has hitherto been complete reciprocity."

The Report is a lengthy document of 96 pages and, in parts 2, 3, and 4, contains matter with much of which, I think, Members of the Section will be in agreement, especially that dealing with the preferential treatment of medical students over midwives in the allocation of beds in the medical schools, and that calling attention to the large amount of clinical material used by midwives who do not intend to practise.

The two parts "1" and "5" are those which most nearly concern the Section of Obstetrics and Gynæcology, and I think they merit our serious consideration.

Part 1.—Historical Survey: The Report mentions the pioneer work of the Obstetrical Society of London (now the Section of Obstetrics and Gynæcology of the Royal Society of Medicine) in laying down rules of practice and conduct, in instituting a voluntary examination for midwives, and the issue of a diploma

guaranteeing that its possessor was "a skilled midwife, competent to attend natural labour." The Report might well have pointed out the historical fact that it was to the persistent efforts of the Obstetrical Society of London that the Midwives Act 1902 was due, and that the first rules and regulations of the Central Midwives Board were not only, as stated in the Report, "no doubt largely based on," but were in many cases worded identically with those of the Obstetrical Society of London. The record of the work of that Society in this connection is to be found in its minute books and *Transactions* (vols. 16, 17, 19, 20, 21, 23, 26, 27, 28, 34, 36, 40, 47).

In volume 36 (1895) an admirable account of the midwives question and of the history of the Obstetrical Society's work in connection with it, up to that date, is given in the inaugural address of the President, Dr. (now Sir Francis) Champneys, Chairman of the Central Midwives Board, who took a leading part in the work of the committee (of which I was secretary) which drew up the rules and regulations to be observed by midwives, published in the Obstetrical Society's *Transactions*, vol. 40 (1898).

*Rules and Regulations of the Central Midwives Board.*—The Report states (p. 55) that the rules and regulations of the Central Midwives Board "appear to have suffered, as is natural, from piecemeal attempts at alteration designed to meet circumstances and cases arising from time to time," and that "the existing rules have, in fact, been severely criticized in evidence. They may be justly characterized as in parts deficient, in parts diffuse, in parts meticulously detailed."

This would appear at first sight to be a sufficiently comprehensive criticism of the rules, calling for suggestions for their improvement. These are forthcoming in Appendix B: but all they amount to is:—

Rule E 1.—Division into two parts, or the use of an asterisk.

Rule E 12.—Amplification; indication of normal frequency of visits and time necessary properly to carry out nursing duties.

Rule E 12A.—Transfer of note to rule.

Rule E 13 (defining normal labour).—Deletion.

Rule E 21.—Revision; transfer of note to rule; use of bold or leaded type; change of punctuation; "indication to direct attention to cases in which disproportion exists between the head and the pelvis"; addition of cases of inefficient uterine action and of breech presentation in a primipara.

These suggestions seem to show that the Departmental Committee did not find much amiss with the present rules and regulations of the Central Midwives Board.

Part 5.—Administration: The Departmental Committee proceeds to make proposals "of some moment"—(1) for the diminution of the number of members of the Central Midwives Board, and the limitation of the Board's functions to those which "besides keeping the Roll, would then be mainly disciplinary and examining"; (2) for the assumption by the Minister of Health of the sole responsibility for approving and inspecting training institutions and teachers, and of laying down the lines of the curriculum of training.

I hope that the Section of Obstetrics and Gynæcology of the Royal Society of Medicine will express its disapproval of both these proposals on the grounds that the Central Midwives Board is an independent body on which expert teachers of midwifery should be well represented, that the Central Midwives Board has performed its duties well, and that this Section does not think that those duties can be equally well performed by the Ministry of Health, whose treatment of the panel doctors under the National Insurance Acts has been characterized by the Lord Chief Justice of England as "pure despotism."

**Dr. Watts Eden** said that the administrative changes proposed in the Report of the Departmental Committee would transfer the control of the training and education of midwives, and also the duty of approving and of inspecting all training

institutions for midwives, from the Central Midwives Board to a Government Department, viz., the Ministry of Health. The Central Midwives Board, though not perhaps an ideal body for the purpose, was composed, for the most part, of those who had practical knowledge of the teaching and practice of midwifery. The exceptions were the members appointed to the Board by the Ministry of Health. As the staff of the Ministry had no practical knowledge of midwifery themselves, it was proposed to appoint an Advisory Committee to assist them in the duties they were to take over from the Central Midwives Board. He had not a scrap of faith in the Advisory Committee. The Ministry already had a strong Medical Advisory Committee which was appointed soon after the creation of the Ministry. He had been informed that this Committee had never had any serious work to do, and had not met for a very long time. The same fate would probably overtake the Advisory Committee proposed by the Report.

It was most important to insist on the recognition of the principle that the control of midwives' education and employment should remain in the hands of an authority appointed for the purpose, upon which doctors and midwives should be strongly represented and should be in a clear majority. The general effect of the proposed changes, including the setting up of a national maternity service, would be to take four-fifths of the midwifery of the country out of the hands of the medical profession and put it under the control of a Government Department.

**Dr. J. S. Fairbairn** said Members should know that the reports of such a Committee could not carry much weight, for they were more "departmental" than authoritative or representative. Its appointment, terms of reference, membership and chairman were determined by the Department—nominally its Minister, to whom it reported and who decided whether the reports should be published or not. When asked to serve, no information was given as to the folk with whom one was to be associated and the first knowledge obtained on this point was when the names were published in the press. Hence he would have no hesitation in criticizing the selection, and the Members of this Section present could look at the names of those on the Committee and decide for themselves whether they carried confidence. They consisted of seven medical and six non-medical persons; four of the medical members and one of the non-medical, i.e., five in all, were whole-time officials. The midwives, the body most concerned, had no representative except one registered midwife who had interested herself in a training school but had not practised. Another important point was that evidence was heard in private and was not published. He would take the recommendations now under discussion as a sample of "departmental" methods, though the memorandum of reservation left little to be filled in. The London County Council was made the mouthpiece, but though the voice was that of its Maternity Committee, the words were clearly those of its medical officer of health, who was not experienced in the administration of the Midwives Acts, and neither he nor the Committee had had anything to do with the training of midwives. From a study of the Report it was difficult to find any justification for these recommendations. The Report chiefly relied on the absence of "inspections" by the Central Midwives Board, yet, as Dr. Watts Eden had said, it was the department itself which had put the Poor Law Hospitals in a privileged position and kept them outside the power of inspection by the Board. Would it not be unfair to begin regular inspections until all training schools could be treated alike? Other instances might be given—did time allow—of privileges accorded to the Poor Law Hospitals and forced on the Central Midwives Board by the Ministry of Health, either under its present name or its former one of the Local Government Board. They form an irresistible argument for the need of an independent body having charge of training and training schools, not for a Government Department interested in the large number of schools under local government authorities. He

could not wonder at the London County Council playing the departmental game, for it was itself an interested party which might be looking forward to some return for its services in the shape of a continuation of past favours to the many training schools shortly to be under its charge. He (Dr. Fairbairn) hoped that this Section of the Royal Society of Medicine, as the lineal descendant of the old Obstetrical Society—which had done more for midwives than any Local Government Board or Ministry of Health—would unanimously accept the resolutions submitted by the Council. In conclusion he would give his view of the recommendation to hand over the profession of the midwife to the Ministry of Health, in the words of the Lord Chief Justice, in his recent book on "The New Despotism": "The conclusion is irresistible that it is manifestly the offspring of a well-thought-out plan, the object and effect of which are to clothe the department with despotic powers."

**Professor Louise McIlroy** asked if 75% of the midwifery cases in the country were to be in the hands of midwives, who would look after the other 25%—specialists or general practitioners?

Teachers were concerned chiefly with the training of students in midwifery and not with that of specialists after graduation.

If general practitioners were not going to practise midwifery, the money spent in their training by medical schools might as well be saved. Owing to the seriousness of this question to teachers and practitioners, this Section should take an active part in the controversy.

The midwives' service had been efficient because it had had the advantage of the training and teaching of specialists. She believed that the retention of the Central Midwives Board would make for a better service for the country than any Government organization.

**Dr. W. H. F. Oxley** said he would remind Members that the committee on Maternal Mortality and Morbidity was still sitting, and was anxious to explore the large subject of its deliberations from every point of view, so that if the Section thought well they could embody their resolutions, if passed, in their reply to the request already sent to them by that committee.

Any evidence would be carefully considered in its relation to the reduction of maternal mortality.

**Dr. James Young** (Edinburgh) said that the report contained suggestions which were timely and valuable, and which if carried into practice were calculated to lead to an improvement in the status and training of the midwife, and to a raising of the general standard of the maternity service of the country. He believed the Report had served a useful purpose in pointing to the need for a national maternity service, and he agreed with its suggestions that State aid was required to ensure that proper supervision of pregnancy and adequate attendance during and after labour could be provided for women generally. He agreed with the previous speakers, however, that the suggestions made in the Report to the effect that the direction of the curriculum and the training of the midwife should be removed from the Central Midwives Board and handed over to the Ministry were harmful and should be resisted strenuously. He believed that the arguments against this procedure which had been stated in the reservations over the names of Dr. Fairbairn and Mrs. Bruce Richmond were irrefutable.

*Resolution.*

The following resolution was put from the Chair and carried unanimously:—

"The Section of Obstetrics and Gynæcology of the Royal Society of Medicine, having discussed the Report of the Departmental Committee on the Training and Employment of Midwives, is of opinion:—

"1. That the responsibility for the education and training of midwives, including approval and inspection of training schools, be retained in the hands of an independent body appointed for the purpose and consisting largely of those who are or who have been engaged in the teaching and practice of midwifery.

"2. That the proposal contained in the Report to limit the power of the Central Midwives Board and to give the Ministry of Health the sole responsibility of approving and inspecting training institutions and teachers, and of laying down the curriculum of training, would, if adopted, be prejudicial to the teaching and practice of midwifery in this country.

"3. That the Departmental Committee responsible for the recommendations to which we take exception was not a representative body inasmuch as it contained only one member out of thirteen who had practical knowledge both of the teaching and practice of midwifery, and this member dissented from the main recommendations of the Committee."

# Section of Medicine.

President—Dr. R. A. Young, C.B.E.

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[*October* 22, 1929.]

## DISCUSSION ON DISEASES OF THE PITUITARY BODY.

**Dr. W. J. Adie:** We classify the common tumours of the pituitary body, the adenomas of the anterior lobe, according to the way their cells stain. The terms chromophil and chromophobe are probably familiar to you: I wonder if they mean the same thing for all of us.

One author, in a book on the ductless glands, states that "the cells of the anterior lobe are divided into 'chromophil' and 'chromophobe,' according to whether they stain with chrome salts or not"; chrome here means chrome, not colour, and chromophil is the same as chromaffin. I have looked at some sections that had been mordanted in Müller's solution for three days; I could see no granules in any of the cells and I feel sure that this confusing statement is wrong.

Benda describes three kinds of cells, those that stain intensively with acid dyes (acidophil cells), those that hardly stain at all with acid dyes (chromophobe or Hauptzellen, the principal cells), and those that stain with basic dyes (basophil cells). A recent author has written that "the cells in the posterior part of the tumour are almost all large basophil elements (chromophobe cells or Hauptzellen)," and this tendency to make chromophil and acidophil synonymous is noticeable in many papers. Red, then, is a colour, and cells that stain red are chromophil, but blue is no colour at all, and an unpleasant name, chromophobe, must be given to cells that are fond of it. To avoid confusion I shall use the terms acidophil and basophil for the cells with granules that stain red or blue with, say, Mallory's acid fuchsin aniline blue, and indifferent for the agranular principal cells, the Hauptzellen that hardly stain at all. And I shall speak of the tumours as granular-celled and agranular-celled, or, for short, granular and agranular adenomas, thus avoiding the confusing terms chromophil and chromophobe altogether.

The tumour associated with acromegaly is usually a simple granular adenoma of the anterior lobe; malignancy is extremely rare. The granules in the cells composing it are nearly always acidophil, sometimes they are all basophil, sometimes they are mixed. I am inclined to believe that the cells are more likely to be basophil in acromegalics who have become obese or cachectic. I notice a tendency on the part of some writers to make their cases fit into a scheme: an acidophil adenoma is always associated with acromegaly or giantism, an agranular adenoma causes obesity and other defect symptoms, a mixed tumour gives a mixture of symptoms. The formula is too rigid. It is certain that every acidophil adenoma does not cause acromegaly; in one of my patients, a woman with a pure acidophil adenoma, headache and diabetes insipidus were the only symptoms; there was not a trace of acromegaly. In another, a grossly acromegalic woman, the cells were agranular and stained indifferently. Mixed granular and agranular tumours are sometimes found in patients with preponderating defect symptoms and some traces of past slight acromegaly, but with some mixed tumours no such traces are found. On the whole, then, we can say that there is a rough agreement between structure and symptoms but that no rigid formula is universally applicable.

Of the signs in acromegaly I shall merely say that they may appear before the tumour is large enough to deform the sella and are almost always obvious before it begins to cause visual or other troubles by pressure on neighbouring structures. This has given rise to an impression, very dangerous to our patients, that a tumour of the pituitary body is necessarily accompanied by signs of ductless gland disorder. I cannot too strongly emphasize the fact that the commonest form of tumour may be very large and cause failure of vision when glandular symptoms are absent or slight.

Of the metabolic disturbances I mention only one—glycosuria. It is noteworthy that persistent glycosuria, so far as I know, occurs with granular adenomas only, that is to say, in giants and acromegalics, and in my experience it only occurs in advanced cases. In many ways it resembles pancreatic diabetes; I have seen an acromegalic, in pre-insulin days, die in diabetic coma; on the other hand, I have a patient who needed twenty units of insulin daily for two years, but has been sugar-free for the last three months without insulin; this variable course is characteristic of pituitary diabetes. It is improbable that it is due to secondary changes in the pancreas, as this organ has been normal in almost all the cases that have been examined after death. I leave for discussion the subject of sugar metabolism in pituitary disease.

A knowledge of the course of the disease is necessary as a guide to treatment. I know several acromegalics in whom the disease has been stationary for years, and others in whom the headaches have ceased, the visual fields remain the same, and feelings of exhaustion and general ill-health have disappeared, although the body continues to increase in size. I cannot advise an operation in these cases, although I know that delay will increase the danger if an operation has to be carried out later. We operate at present to relieve headache and conserve vision. Should we operate in the earliest stages of the disease in order to prevent the deformities?

Some day, soon probably, we shall be able to prevent any ill-effects that may result from surgical removal of the gland, by substitution therapy; at present I do not think it is justifiable to operate for the glandular disturbances only. X-ray treatment should always be tried in acromegaly; it is of little or no value in other forms of tumour and radium has not given good results.

For every case of pituitary tumour I see with acromegaly, I see five or six without it. Of all disorders of the pituitary body, this one, adenoma of the anterior lobe without acromegaly, is not only the commonest but by far the most important. It is confined almost exclusively to adults. The cells composing it do not take on either acid or basic dyes; it is an agranular adenoma. The cardinal sign is loss of vision, there may be nothing else. This is the only statement I make to-night to which I attach great importance. Eyesight is precious; we get few chances of saving it; this is one of them; but it is often lost because these tumours are not diagnosed in time.

In most of the cases there is a definite tendency to adiposity, the skin is smooth, pale and soft, and the hair scanty; in women the periods cease, in men desire and potency diminish; the optic nerves are pale, the fields show bitemporal defects, the sella turcica is greatly enlarged and the patient has headaches. But endocrine symptoms may be absent or slight; there may be no headache; the optic nerves may be normal, the field defect may be of almost any form, and X-rays may show a normal sella. It will be gathered from this that the diagnosis may be difficult. My point is that pituitary tumour should be suspected in every case of failing vision without an obvious cause. I go further and say that we should search for a pituitary tumour even when some other cause seems to be present. For in the case of pituitary tumour something can be done; optic atrophy from other causes is usually hopeless. Toxic amblyopia is diagnosed too readily and valuable time is wasted while harmless septic foci are being sought for and removed.

The commonest cause of progressive optic atrophy in adults is tabes, but a pituitary tumour may cause not only optic atrophy, but loss of tendon reflexes and pains in the legs—pituitary tabes as it is called. We must therefore scrutinize every case of alleged tabetic optic atrophy very carefully. If the atrophy is due to tabes, the pupils will show the Argyll-Robertson phenomenon even in the earliest stages. If it is due to some other cause, although vision may be grossly defective and the discs pale, the pupils will probably still react to light. This rule helped me in a case which had been diagnosed as tabes in a woman with severe optic atrophy and a positive Wassermann reaction. The pupils reacted to light and further investigation led to an operation on the tumour that restored the patient's vision.

Third, in order of frequency, come the tumours that arise from the remains of Rathke's pouch and from groups of cells on the stalk—congenital cystic tumours, supra-sellar cysts, Rathke's pouch tumours, hypophyseal stalk tumours, para-hypophyseal tumours—these are some of the names that are given to them. Apart from very rare exceptions, these are the only tumours that produce symptoms before the age of fifteen. In a characteristic case the patient is an intelligent and cheerful child, rather short for his years, with gross signs of endocrine disorder. He is probably obese, with small genitals, but he may be emaciated, dwarfed or prematurely senile. He has come to us, not for these troubles, but because he is now getting headaches and his vision is failing. The discs are swollen, the fields show a bitemporal defect, and the sella is deformed with shadows above it due to calcification in the walls of the cyst. Perhaps there is a history of attacks of urticaria, of several attacks of "measles" or of other rashes. But failing vision, with or without general symptoms of increased intracranial pressure, may appear at any age, even as late as the fifth decade, in patients entirely free from endocrine symptoms. Papillœdema is common in young patients (it hardly ever occurs with any other form of pituitary tumour) but in older patients optic atrophy is the rule. Homonymous field defects and scotomata are common, and the very helpful supra-sellar shadows are often absent. In children, however, the diagnosis is usually correctly made; in adults it is often impossible to distinguish these tumours from the common agranular adenoma without acromegaly. These congenital cystic tumours are unfavourable for operation and the ultimate prognosis is bad.

The symptoms in the cases I have described fall into two groups: those caused by the pressure of an intracranial tumour—these are the more important at present; and those caused by the disordered function of a ductless gland—these are perhaps of greater academic interest.

Time will not allow me to consider the pathology and symptoms of pituitary diseases other than tumours, or to discuss the various manifestations of pituitary disease separately, but I should like to say something about one of them, diabetes insipidus, because what I say about the development of our knowledge of this symptom and the unsolved problem concerning it can be applied with slight changes to all the rest.

Is diabetes insipidus ever a symptom of uncomplicated pituitary disease, or is it always, as some say, the result of damage to neighbouring nervous structures in the hypothalamus? How do the structures that control water metabolism normally act? Is their influence exerted along nervous channels, or by hormones? Is diabetes insipidus an expression of hyperfunction or of hypofunction of the controlling mechanism? Can it be attributed to hyperfunction or to hypofunction of one of the anatomical divisions of the pituitary body? Is it a simple symptom or is it a complex, an algebraical sum of disturbances of simple functions, and thus capable of occurring in fragmentary forms? Do its clinical features vary with the site of the lesion producing it? Can the disturbance be corrected by giving extracts of the pituitary body? And so we might go on multiplying questions that would apply equally well to any symptom of pituitary disease.

Some of these questions have been answered; most of them are still open for discussion. About ten years ago I saw a boy with diabetes insipidus which came on immediately after he had been wounded while practising bayonet fighting. The blade had passed along the floor of the orbit, divided the optic nerve and, presumably, damaged the pituitary body or the floor of the brain. It was a case similar to this, in that it was traumatic (a bullet lay just above the sella) that caused Frank to suggest for the first time that diabetes insipidus was caused by damage to the pituitary body. Thereafter, cases were described in which tumour, gumma, tuberculoma, hæmorrhage, or inflammation, in the pituitary body had caused this symptom, and when van der Velden showed that an injection from the posterior lobe checked the polyuria, the view that diabetes insipidus was due to loss of a secretion normally produced by the posterior lobe, seemed to be fully confirmed. The objection that this symptom was often absent when the gland was destroyed and that it might disappear in the course of time was met by Hann who proved that polyuria only occurred so long as the anterior lobe was still intact or almost so.

But the pure hypophyseal view did not prevail for long. It was known that polyuria could be produced experimentally by damage to a certain part of the medulla, and the existence of direct nervous connections between this spot in the medulla and the nuclei in the wall of the third ventricle suggested that injury to these higher centres might produce the same result. As we now know, it does so. Carried away by their success, those who first obtained this result rejected the hypophyseal view entirely and held that diabetes insipidus was always due to a lesion of the hypothalamic centres; polyuria after removal of the pituitary body was due to accidental injury to these centres, and polyuria in pituitary disease was due to pressure upon them.

I need not dwell upon this long controversy as we know now that neither extreme view was correct. A patient of mine who had had her breast removed for cancer came to me with diabetes insipidus. She had a secondary deposit of carcinoma in the posterior lobe of the pituitary body. This convinced me that polyuria *can* occur with a lesion confined to the pituitary body. This may be compared with the definite syndrome, Simmonds' disease, that occurs with destructive lesions of the anterior lobe, and the defect syndromes that arise from simple aplasia of the gland where there is no question of damage to the hypothalamus.

On the other hand, there is no doubt that experimental lesions strictly confined to the hypothalamus can produce diabetes insipidus, also the lesions of disease as in, for example, encephalitis lethargica. I think we may safely conclude that the answer to my first question is definite: diabetes insipidus *can* result from a lesion confined to the pituitary body, it *can* also result from a lesion confined to the hypothalamus. The gland and the adjacent centres form an intimately connected system; they act together as a neuro-endocrine mechanism in some way as yet unknown, and damage to one or the other part of this system may produce polyuria. The same is probably true of all the symptoms that occur in disease of this region.

If now we ask ourselves how this mechanism acts, we find that we are approaching the limits of our knowledge. Nervous? or hormonal?—that is the question. One suggestion that still crops up from time to time is that secretions from the glands pass into the cerebrospinal fluid in the third ventricle, and thence, in some way, influence the hypothalamic centres. For this view there is not a scrap of evidence that will bear close scrutiny. It is certain that injury to the tuber can produce polyuria, although the gland is intact. This suggests that the nervous centres are the predominant part of the system. Further, injury to the tuber still produces polyuria in an animal from which the gland has been removed. This occurs when the kidneys have been completely denervated; hence we are forced to conclude that a lack of nervous impulses normally conveyed from the periventricular nuclei to the medulla and by the splanchnic nerves causes metabolic disturbances in the tissues that lead to polyuria.

No one, so far as I know, has tried the experiment of dividing the cervical cord and then injuring the tuber. If polyuria did not occur under these conditions, that fact would support the purely nervous theory. Professor Verney's ingenious experiments with a heart-lung-kidney preparation favour the notion of the existence of an anti-diuretic hormone, but the bulk of the evidence is strongly against it. All we can say at present is that the normal metabolism of water and salt in the body seems to depend upon the harmonious interplay of the pituitary body and hypothalamic centres; of the mode of action we know little or nothing.

As a clinician I have been struck by certain differences between the diabetes insipidus of pituitary origin and that due to tween-brain disease. In a word, the former is milder; the desiccation and emaciation of tween-brain cases do not occur with polyuria of pituitary origin, and temporary deprivation of water is better borne. Further, the biochemist is teaching us that the amount and concentration of chlorides in the blood and urine differ greatly in different cases, that abnormalities of salt metabolism may be present before polyuria appears or after it has ceased, and that isolated metabolic disturbances may be present without polyuria or other symptoms in disease or injury of the pituitary region. I shall not elaborate this, but merely say, first, that polyuria is certainly not a simple symptom; it is the complex sum of a number of disturbances of simpler functions of vegetative centres; and secondly that clinical and chemical observations, though scanty, suggest that the features of polyuria differ with the site of the lesion that causes it.

For the elucidation of the symptom I have chosen for special reference the clinician and the biochemist must work hand in hand; until we know more of the metabolism of water, that most wonderful of chemical substances, it is unlikely that we can finally solve any of the problems of growth and metabolism. It is to the biochemist and the experimental physiologist, then, that we look for the advances that will lead to a better understanding of the nature and mode of production of the symptoms in diseases of the pituitary body.

**Mr. Norman Dott** said that from the surgical point of view he would group the subject under three heads: (1) Distinctive types of pituitary tumour cases which present themselves for surgical treatment; (2) the nature of the treatment he had found most applicable to these types; (3) the results of such treatment.

For this purpose he had selected seven particularly clear-cut examples from his own cases. They illustrated (*a*) simple hypopituitarism as it affected the child and the adult; (*b*) what we must now call "eosinophil" hyperpituitarism with acromegaly; (*c*) pure hypothalamic disturbance with adiposity, polyuria and somnolence; (*d*) pure visual disturbance without pituitary or hypothalamic signs and without local bony deformation; (*e*) a combination of several of these disturbances. Incidentally, these cases would illustrate the transfrontal and trans-sphenoidal methods of operation and radiotherapy as applied appropriately to the various lesions.

[Mr. Dott then described seven cases bringing out these features, and showed a series of lantern slides demonstrating the physical types in various pituitary disturbances, the gross and microscopical characters of the lesions encountered at operation, the operative procedures employed and the striking degree of the visual recovery obtained. Particular stress was laid on the absence of deformity after these operations.]

Mr. Dott, in demonstrating a case of acromegaly, said that evidence had now accumulated showing, with practical certainty, that the "eosinophil" cells were concerned with growth and, with a high degree of probability, that the "basophil" cells were concerned with sexual development and activity. It had been found that acid and alkaline extracts of the anterior lobe affected these factors specifically and

independently in experimental animals. Thus, in relation to the "eosinophil" hyperplasia associated with acromegaly, it was now desirable to use some such expression as "eosinophil hyperpituitarism," indicating that this particular gland element was in excess and in a condition of hyperfunction, in preference to the formerly accepted term "hyperpituitarism," which, in the light of modern knowledge, was not sufficiently specific. Sexual function might or might not be depressed in acromegaly; it usually was so in the later stages when the grandular swelling had attained a considerable size. In acromegaly this symptom presumably depended on whether the basophil cell element of the anterior lobe was more or less crowded out by the hyperplasia of the "eosinophil" cells.

There was need for a revision of nomenclature in connection with the cell types of the anterior lobe. These cells were named according to particular stains which their granules were supposed to absorb or according to the supposed chemical reaction of the granules. Dr. Adie, in opening, had cast doubt on the constant association of an increase of "eosinophil" cells in the tumour with acromegaly. In Dr. Adie's experience the cells in such tumours were always granular, but did not always stain with eosin. He (the speaker) thought that the discrepancy between his own findings and those of Dr. Adie was not a discrepancy of fact but of nomenclature, and depended upon the fixing and staining methods used. Some years ago, writing from the clinic of Dr. Harvey Cushing, in association with Dr. Percival Bailey, he had suggested that the granules of the pituitary cells should be described as "alpha" and "beta" granules, and should be identified by certain specific fixing and staining methods. Ordinary methods of fixation and staining did not give reliable information as to the nature of the granules, and the terms "eosinophil" and "basophil" were misleading and highly objectionable if taken in their literal sense. As a matter of fact both types of granules stained most specifically with dyes belonging to the acid class. By using specific staining methods he (Mr. Dott) had not failed to identify "alpha" or "eosinophil" granules in the cells of the tumours in more than fifty cases of acromegaly. Probably the difference of opinion on this subject was due to the employment of insufficiently specific staining methods.

With regard to treatment, it was unfortunate that arguments should be advanced in favour of one or other operative or radiotherapeutic procedure in relation to pituitary tumours in general. Judging from his own experience, he thought that in early cases of adenoma, whether of the "alpha" or of the non-granular cell type, radiotherapy alone should be employed initially. There had not yet been sufficient time to warrant an estimate of the final results of this procedure, but there was reason to believe that it might control the situation satisfactorily. For the more usual cases of adenoma in which the patient sought advice because vision was already impaired and endangered, immediate mechanical relief of pressure by the simple trans-sphenoidal operation was indicated and should be followed by radiotherapy to inhibit or destroy the remaining fragments of the growth. In the case of adenomata with evidence of extensive intracranial expansion, and in all cases of parahypophyseal tumours, a transfrontal operative procedure was obviously required. It would be appreciated that the choice of the most appropriate treatment for a given case demanded an accurate clinical diagnosis of the exact relations and pathology of the lesion. Such a diagnosis was usually quite possible.

Results were, on the whole, very encouraging and satisfactory. As in most other conditions, they depended largely on the degree of advancement of the disease at the time when the patient sought advice. The optic fibres if not too long or too severely compressed, possessed a remarkable power of recovery. Malignancy was extremely rare in pituitary tumours, and the results, on the whole, compared quite favourably with those of most other major surgical procedures.

**Professor E. C. Dodds:** The connection between the anterior lobe secretion and growth has been known for many years, and its association with the development and control of the sex organs was demonstrated by Fröhlich in 1901. It is only recently, however, that direct experimental evidence has been obtained on the subject from physiologists and biologists. Previously we had to rely mainly on the public records of rare cases in which the glands were involved in some pathological condition. It may be well to summarize briefly the prevalent views regarding the internal secretion of the anterior lobe of the pituitary, including only those observations of which there is abundant proof. With regard to the question of growth, there have been many claims to the production of giant rats and other animals by the administration of extract of the anterior lobe of the pituitary, and in the year 1921 the American workers, Evans and Long, published an account of their researches. They showed that if a specially prepared extract of the anterior lobe of the pituitary was administered intraperitoneally into very young suckling rats, these animals grew at a much greater rate than their untreated brothers and sisters. When puberty was reached in the treated animals, it was found that the growth rate did not slow down, as is the case in normal animals, but continued to rise sharply until in the final stages animals were produced of twice the weight of the controls, and twice the weight of any other rats of the same breed. By means of a long series of researches, involving the transplanting of the pituitary gland subcutaneously into immature animals, Zondek and Smith and Engle were also able to demonstrate the importance of this lobe in connection with the development of the sexual organs. Thus if to a young, immature animal a subcutaneous anterior lobe transplant is given, sexual maturity is reached at a much earlier age than in the untreated animals. If, on the other hand, extracts of the anterior lobe, prepared in certain definite ways, are injected subcutaneously into animals before the age of puberty, a very interesting series of events takes place. Thus, in the female mouse it is possible to develop corpora hæmorrhagica and, mainly, corpora lutea enclosing undischarged ova (so-called corpora lutea atretica). The hormone in urine, however, produces mainly corpora hæmorrhagica within some fifty-six hours. In addition to this, the signs of puberty develop, the vagina, which was originally a solid cord, opens, and œstrus may supervene. If, on the other hand, this extract be administered to a normal adult animal it is found that the œstrus reaction is inhibited. This has been explained in the following fashion: the anterior lobe of the pituitary secretes a hormone which travels in the blood-stream, part of which is necessary for the normal growth of the animal, the other part being responsible for stimulating the ovaries into activity. This is shown by the development of corpora lutea, and by the stimulation of the ovary to secrete the œstrus-producing hormone, which, in turn, causes the signs of puberty. If, however, the anterior lobe extract be administered either continuously to such an animal, or to an adult animal after puberty, œstrus disappears; thus it is assumed that the hormone stimulates the ovary to produce œstrin at such a rate that it is rapidly exhausted and the result is the disappearance of the œstrus. It follows, therefore, from what has been said, that the sexual part of the hormone of the anterior lobe of the pituitary actively controls ovarian function, that is to say, it is this extract which is responsible for the sudden activity of the ovary at puberty, and also for the formation of corpora lutea. In addition it has been shown to be essential for ovulation, as the experiments of Parkes and his co-workers have proved that if the pituitary gland is removed, ovulation and rupture of the follicle will not occur in a rabbit following coitus. Again, the experiments of Zondek and Ascheim have shown that in pregnancy there is a remarkable increase in the production of this pituitary secretion. This is evident by the fact that it is secreted with the urine in the very early stages of pregnancy and continues right on until delivery. A careful series of observations shows that the appearance of this hormone in the urine is diagnostic of pregnancy, and a test has

been based on these lines. Returning to the present problem, it has been found that if the urine of pregnant women be injected subcutaneously into female immature mice, these then develop the signs of puberty in a few days. On killing the animals and opening their abdomens, it is found that the ovaries are covered with little red spots, namely, corpora hæmorrhagica or "blut punkte." The finding of these corpora hæmorrhagica, or of corpora lutea, is the diagnostic part of the test; the development of puberty as shown by the appearance of œstrus must not be taken as evidence that the patient is pregnant. In the urine of pregnant women there also occurs another hormone, namely, that produced by the ovary, called œstrin. Although the appearance of this substance in large quantities in the urine may be strong evidence that pregnancy has supervened, it is not anything like so diagnostic as the luteinizing and hæmorrhagic principle of the anterior lobe. Thus œstrin has been found in the urine of non-pregnant women in certain conditions and, in addition, appears in male urine. A prolonged professional experience with this test in these laboratories has shown that this is a very reliable means of diagnosing pregnancy.

Up to the present we have only referred to experiments showing the relation between the anterior lobe hormone and the female sexual organs. It is also claimed by Zondek that injections of this hormone will cause the appearance of puberty in immature male animals.

It has therefore been definitely proved that the anterior lobe of the pituitary body secretes the hormones which control growth and also control the activity of the sexual glands. Whether the two principles are separate or not need not be considered here, but it appears from recent evidence that there are at least two, if not three, separate hormones secreted by the anterior lobe. It is a relatively simple matter to test this fluid and excretion for the luteinizing factor of the anterior lobe, and it is interesting to speculate what will result when these new methods of studying the functions of the anterior lobe are applied to various medical conditions. The development of these exact experimental methods of demonstrating the various principles may be applied to such conditions as various disorders of growth, infantilism and mental disorders.

The object of this brief summary of the experimental work done in the field of biology and biochemistry is to call attention to these new methods of investigating pituitary disease and function, and it is hoped that these methods may be used with success in the study of many allied medical conditions.

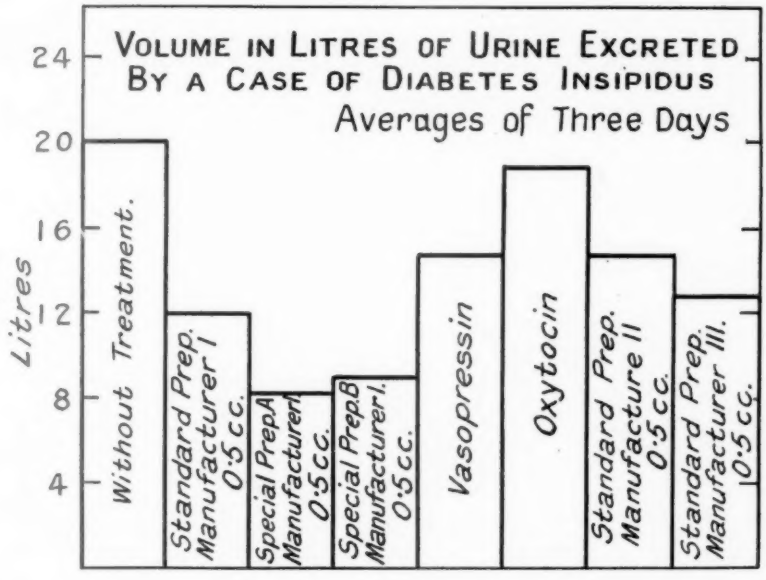
**Dr. O. Leyton** said that he and his assistants had had the opportunity of making a few observations on diabetes insipidus.

Several years ago when a series of cases were under his care, he had tried the effects of different extracts of pituitary gland and found that their potency in controlling diuresis differed greatly, although all the extracts were standardized and contained the same quantity of the substance as that which caused the contraction of the uterus. This led him to the conclusion that the extracts contained at least two different substances, a view recently proved correct by the separation of vasopressin and oxytocin. There remained, however, the problem whether vasopressin controlled diuresis or whether the substance which controlled diuresis was separate from vasopressin, but associated with it when attempts were made to isolate the different bodies elaborated by the pituitary gland.

Recently a case of diabetes insipidus was treated by various extracts. When untreated, the patient excreted 12 litres of urine a day, provided he was allowed to drink as much as he wished. After the injection of a special extract ("A") of pituitary gland, ½ c.c. at intervals of 12 hours, the excretion fell to 8 litres. This extract had been prepared from fresh pituitary glands and the time taken between the preparation of the extract and the death of the animal was as short as possible.

If the glands were kept one hour the effect as shown on the chart was slightly less, and if that time was exceeded, the efficiency of the extract fell rapidly. Filtering the extract, too, led to a decrease in its value. The standard pituitary extract was much less active in controlling diuresis; this was prepared from frozen pituitary glands imported from South America, but nevertheless it was better than any other extract which he had tried.

Since the vasopressin solution was said to be two and a half times as strong as the other extracts, $\frac{1}{5}$ c.c. was used instead of $\frac{1}{2}$ c.c. Oxytocin, as expected, had no effect upon the diuresis. Two other extracts were used for comparison.




It would be dangerous to draw any conclusions from a single series of observations, especially since the accuracy with which the vasopressin content of the solutions was estimated, was a vital factor.

Referring to the question as to whether patients who had pituitary tumours and glycosuria were able to burn sugar, he suggested that it might be wise to give to some patients a diet of a known carbohydrate content and note the quantity of sugar excreted; on making a progressive increase in the carbohydrate given, the excretion of sugar might increase proportionately, in which case the power of burning sugar in all probability would prove to be normal. If, the more sugar given, the less was utilized then the condition simulated true diabetes mellitus. Hyperglycæmic glycosuria was not necessarily diabetes mellitus.

**Dr. Macdonald Critchley:** I propose to limit my remarks to the pathology of the epithelial tumours of the pituitary and infundibular regions. In order to explain the histogenesis of these particular neoplasms, it will be necessary to recapitulate briefly the main steps in the development of the pituitary body.

It arises from two separate structures: (1) an oral part which grows up from the primitive stomodœum, and (2) a neural portion extending down from the forebrain. At a very early stage an invagination occurs in the buccal ectoderm, which is known as the pouch of Rathke. This pocket deepens, and the orifice later narrows to form the craniopharyngeal canal, which then elongates to become the cranio-pharyngeal duct. Later still the buccal part of the duct disappears, but the deeper portions persist. By the fourth week Rathke's pouch has come to lie in close apposition to a down-growth or the floor of the diencephalon, called the infundibular process. The cells of the anterior aspect of Rathke's pouch proliferate rapidly so as to form the pars anterior of the adult pituitary body. Cells in the posterior aspect increase to form the pars intermedia. It is interesting that the eosinophil type of cell does not appear until much later, namely, the ninth month of fœtal life. The original cavity of Rathke's pouch persists as a narrow cleft which is often visible between the anterior and intermediate lobes. Two lateral

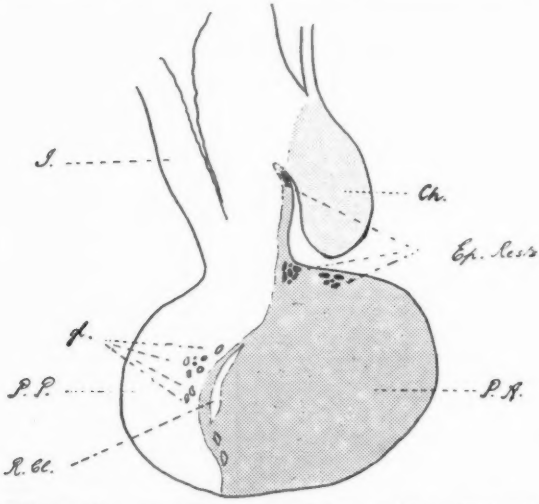



FIG. 1.—Semischematic representation of the pituitary and infundibulum (after Erdheim). (*I.*) Infundibulum, showing remnants of the primitive infundibular process. (*Ch.*) Optic chiasma. (*P.P.*) Pars posterior, containing glandular elements at *gl.*, representing ingrowths from the pars intermedia. (*R.Cl.*) The intraglandular cleft, or Rathke's cleft. (*P.A.*) Pars anterior. (*Ep. Rests.*) Epithelial anlage, representing remains of the embryonic craniopharyngeal duct.

processes bud off from the pouch and grow upwards along the stalk so as to constitute the lobulus bifurcatus, the "lobule of the stalk," or the pars tuberalis of Tilney. Meanwhile the cells of the infundibular process have been increasing in number so as to develop into the pars posterior anteriorly, and the infundibulum or stalk posteriorly. Within the adult posterior lobe there are usually to be seen scattered chromophobe cells representing inclusions of tissue from the pars intermedia. Remnants of the primitive cavity of the downgrowth from the forebrain survive as the "infundibular recess" at the cephalad extremity of the stalk (fig. 1).

The epithelial types of hypophyseal tumour take origin in one of two sites: some of them spring from the primitive cavity of Rathke's pouch, that is, the cells lining the intraglandular cleft. Most of them, however, arise from embryonic remains of the former craniopharyngeal duct which may exist, as Luschka first showed, in the vicinity of the normal pituitary body. Erdheim was able to demonstrate epithelial rests lying in relationship with the infundibulum, in ten out of thirteen adult pituitaries. These relics are found in two chief sites, viz., the upper and lower extremities of the anterior aspect of the hypophyseal stalk. It is probably from these rests that the majority of epithelial tumours develop (fig. 2).

Following Duffy's classification, one may group the suprapituitary epithelial tumours as: (*A*) Cysts of Rathke's pouch. (*B*) Cranio-pharyngeal duct tumours, consisting of (1) papillary cysts, (2) adamantinomata, (3) spinal-celled or prickle-celled carcinomata.

*A*. This is the only type of neoplasm to which the term "Rathke pouch tumour" is strictly applicable. They are met with as unilocular, colloid-containing cysts, frequently distending the pituitary, though often lying above the main mass of the gland. They are usually described as being lined by columnar or ciliated epithelium, corresponding with the columnar epithelium of the intraglandular cleft.

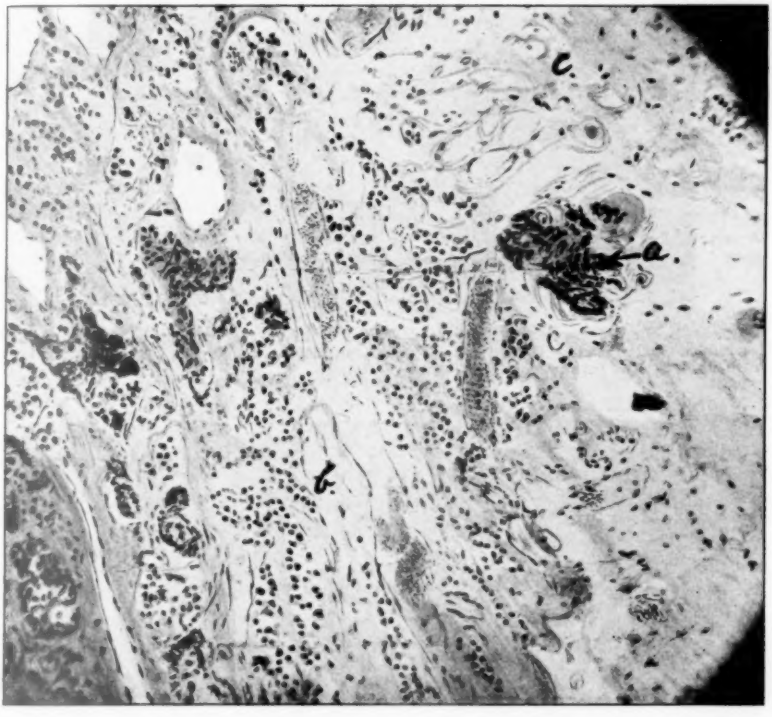



FIG. 2.—Stalk of pituitary with portion of pars tuberalis and also columnar epithelial rests. (*a*) Epithelial anlage. (*b*) Chromophobe cells constituting the pars tuberalis. (*c*) Tissue of infundibulum proper.

As a matter of personal experience, however, it frequently happens that these cysts are lined by stratified or flattened cuboidal epithelium. This is in accord with the type of epithelium found lining Rathke's cleft in both human and mammalian pituitaries; areas of ciliated epithelium, when present, are exceptional and fragmentary. In this connection one may perhaps point out the incorrectness of the statement so often made, namely, that the adult human hypophysis contains no pars intermedia and no intraglandular cleft.

*B*. (1) Under the group of papillary cysts of the cranio-pharyngeal duct are collected a rather heterogeneous collection of semi-cystic tumours, composed of

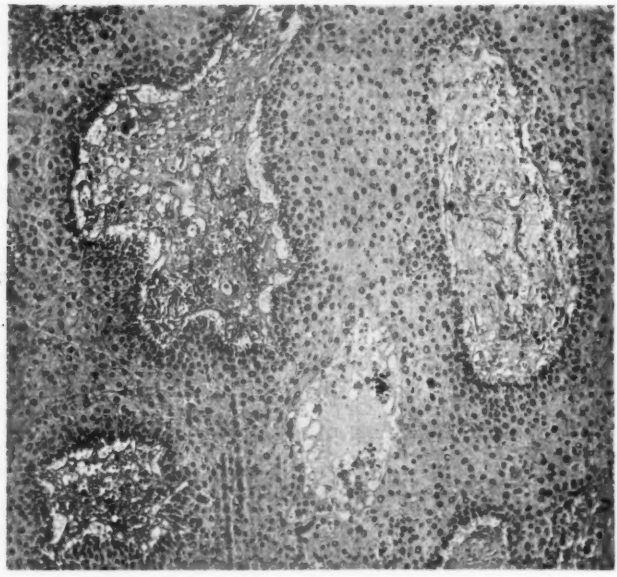


FIG. 3.—Section of an epithelial suprapituitary cystic tumour, conforming to the histological picture of a papillary cyst. (From Critchley and Ironside, "The Pituitary Adamantinomata," *Brain*, 1926, by kind permission of the Editor.)

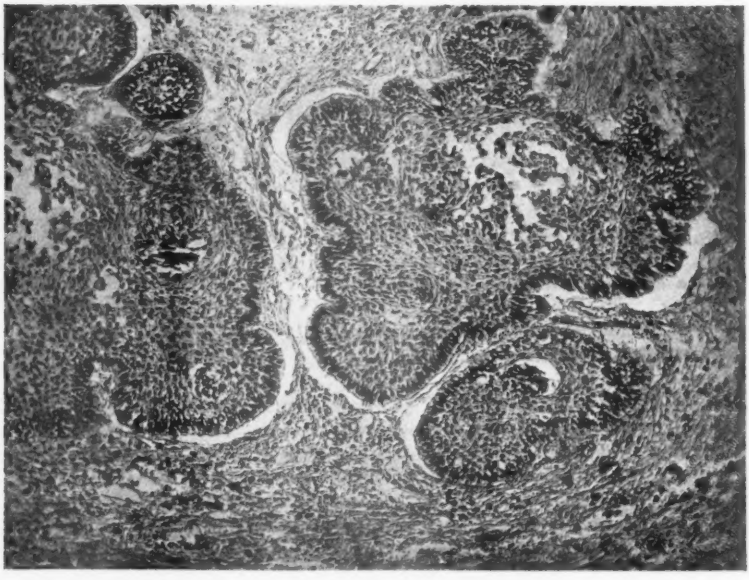


FIG. 4.—Section of a suprapituitary adamantinomata, showing epithelial masses of prickle-cells surrounded by a single layer of columnar cells, arranged in palisade formation and resembling the ameloblasts (adamantoblasts) of the primitive enamel organ. (From Critchley and Ironside, *Brain*, 1926, by kind permission of the Editor.)

branching epithelial columns within a connective-tissue matrix. Such papillomata are formed of stratified, cubical, or transitional types of epithelium. Tumours of this variety are rare. (Fig. 3.)

(2) The adamantinomata are the most frequent and characteristic tumours of the cranio-pharyngeal duct. They comprise a branching epithelial tree as in the papillary cysts, but differ in the character of the epithelium. They are characterized by a single layer of columnar cells arranged in palisades, and surrounding masses of prickle cells. They are named adamantinomata on account of their resemblance to the mandibular adamantinomata or soft epithelial odontomes. The columnar cells strongly recall the ameloblasts (adamantoblasts) of the primitive enamel organ, and it is possible that their presence in the pituitary region is due to embryonic inclusions (the *débris épithéliaux paradentaires* of Malassez) within the buccal ectoderm of the cranio-pharyngeal duct. The pituitary adamantinomata are apt to undergo hydropic degeneration, keratinization, calcification and sometimes ossification. (See fig. 4.)

(3) The third variety of duct tumours, namely, the spinal-celled carcinomata, are excessively rare. They are locally malignant and may also give rise to metastases.

It is possible that yet another type of embryonic tumour may occur in relation to the pituitary body. The infundibular recess, as representing the original cavity of the infundibular process of the fore-brain, may be the origin of certain of the suprapituitary neoplasms, though not, of course, of epithelial nature. Possibly the so-called medullo-epitheliomata of this region may arise from relics of the primitive evagination of the diencephalon which is destined later to form the stalk and pars posterior.

**Mr. Hugh Cairns:** I propose to speak about the differential diagnosis of diseases of the hypophysis from the surgical point of view, basing my remarks on cases which I have personally observed. Some cases are referred to the surgeon because they exhibit disorders of internal secretion, while others—and this is the larger group—come because they present one or more of the so-called "neighbourhood" signs of hypophyseal disease, namely, optic atrophy, bitemporal hemianopsia and enlargement of the sella turcica.

It is scarcely necessary to point out the importance to the surgeon of accurate diagnosis of the diseases of this group. He does not, for example, wish to operate on a case of intracranial aneurysm, under the impression that he is dealing with a hypophyseal tumour. Again, in those diseases of the hypophysis which are definitely surgical in nature, it is necessary to make an accurate diagnosis before operation, in order that the most suitable surgical approach to the lesion may be chosen. Some cases are best approached through the nose by the trans-sphenoidal route, while others should be dealt with from above, through a frontal approach.

Dealing first with that group of cases which exhibit disorders of internal secretion, the physical changes produced by acromegaly are unmistakable, and difficulty in diagnosis is rare. However, I have seen one case, originally diagnosed as acromegaly, which proved on further investigation to be a case of hypertrophic pulmonary osteo-arthropathy, due to a neoplasm of the lung. This patient had enlarged extremities and a rather prominent mandible. The main differentiating feature between these two conditions rests on the fact that in acromegaly the overgrowth is not limited to the acral parts, but is generalized, affecting also such parts as the tongue.

Occasionally acromegalic patients may be found to have a normal sella turcica. The clinical diagnosis of hypophyseal tumour would be difficult, but for the characteristic, though early, signs of acromegaly. In this type of case the tumour

tends to extend upwards, rather than downwards into the sella turcica, and rapid failure of vision may be expected to occur. The field-defect in such cases is often a scotomatous type of bitemporal hemianopsia, of the type which has been so thoroughly studied by Traquair. In a recent case, in which the sella was practically normal, sudden and rapid failure of vision occurred with scotomatous bitemporal hemianopsia. An operation was performed and the tumour was removed by the transfrontal approach. The fields rapidly returned to normal and have so remained since the operation over a year ago. One interesting feature of this case was the shrinking of the hands that is so frequently seen after operation for acromegaly. When this patient left hospital after her operation and began her household duties again she found that the thimble which she had been using for the previous eighteen months was much too large for her. Not only did her hands become smaller, but the unpleasant numbness and tingling of the fingers, from which acromegalics suffer so much, entirely disappeared, and her features became less coarse than they had been before operation.

The next type of case that is often referred to the surgeon as a case of pituitary disease is the so-called Fröhlich's syndrome. I recently saw an excellent example of this condition—a boy aged 11½ years weighing 12 st. His skin was smooth and soft, and practically hairless. The genital development was poor. His only complaint was that of obesity which had begun three years before. The sella turcica was small and there was no suprasellar shadow. Visual acuity and visual fields were normal, as was the rest of the neurological examination. There was slight polydipsia and the carbohydrate tolerance was greatly raised. Thyroid treatment and dieting had been tried without much effect. The cause of the onset of this trouble is quite obscure and there is no evidence that the boy has a tumour. This syndrome is produced by a number of different pathological lesions. In some cases there is a cyst of the cranio-pharyngeal pouch, in others a pituitary adenoma of the chromophobe type, in others a glioma of the third ventricle ; in the great majority of the cases, however, there is no definite surgical lesion of the hypophysis or of adjacent regions. Some of this last group of cases, the "non-surgical ones," have recurrent attacks of petit mal and show mental retardation. Sometimes there is a history of previous head injury or of an illness suggesting encephalitis. These patients rarely die, and, so far as I know, there have been very few post-mortem investigations.

The next lesion to be considered in the differential diagnosis of hypophyseal diseases is the suprasellar cyst (cyst of the cranio-pharyngeal pouch). In my experience this lesion is more often confused with tumours of the posterior part of the third ventricle, or of the posterior fossa, than with tumours of the hypophysis itself, because in the greater number of the cases there are no very obvious symptoms of endocrine disorder. However, occasionally a case is seen which presents bitemporal hemianopsia and adiposity, or stunting of growth. The main differentiating feature in diagnosis is radiological. In 75% of these lesions, calcification can be seen in the skiagrams. A recent case, which was verified at operation, was particularly interesting because the original skiagrams did not show any sign of suprasellar calcification. However, a cranio-pharyngeal pouch cyst was suspected and more skiagrams were taken, with under-exposure of the films, and in that way the calcified parts were revealed, and a diagnosis was thus confidently made.

Suprasellar meningioma or endothelioma is another lesion which has to be differentiated from tumours of the hypophysis itself. It is unusual for suprasellar meningiomas to be calcified or to show in the skiagrams, though when the tumours become large they frequently produce some alteration of the anterior clinoid processes and the intervening optic groove, which shows in the skiagrams. The clinical syndrome in this type of lesion is bitemporal hemianopsia associated with optic atrophy and with a sella turcica of normal size. Another important feature of

the syndrome is that there are no endocrine symptoms, such as one finds in acromegaly or in the chromophobe adenoma of the hypophysis. This tumour is found most commonly in elderly people. The first symptom is failure of vision, and the diagnosis depends in the first instance on testing the visual fields. I have seen one case of chromophobe adenoma of the hypophysis in which the pre-operative diagnosis was one of suprasellar meningioma, because the tumour was rising out of the roof of the sella turcica and had thus produced no enlargement of the turcica. The correct diagnosis was only made at operation. This is a relatively unimportant error in clinical diagnosis, because the surgical approach to this type of adenoma of the hypophysis is the same as for the suprasellar meningioma.

"Meningioma en plaque" near the sella turcica is another type of meningioma which may occasionally give rise to signs simulating pituitary tumour, namely, optic atrophy, defect of the visual field and alteration of the shape of the sella turcica. Unilateral exophthalmos is a fairly constant sign in this type of lesion.

Glioma of the optic chiasm is often confused with pituitary tumours. It produces optic atrophy, occasionally also defect of the visual fields, and some enlargement of the sella turcica. There is also obesity and polyuria and polydipsia. In these cases the enlargement of the sella turcica is apt to be of a distinctive type. The sella turcica is shaped like a pear, owing to the projection of the tumour forward into the optic foramina, which may themselves be shown by a skiagram to be enlarged. The visual disturbance is out of all proportion to the changes in the disc. The patients who have this type of lesion are usually young. They often have spots of brown pigmentation on the skin, a manifestation of von Recklinghausen's disease.

Gliomata of the third ventricle may press down upon the sella turcica and cause it to enlarge. They also produce obesity, polyuria and polydipsia. As a rule, however, they can be distinguished from pituitary tumours by the fact that the papillœdema appears in the early stages of the illness, and by the fact that they do not produce temporal hemianopsia. It is often difficult to distinguish, before operation, between cysts of Rathke's pouch and glioma of the third ventricle, unless there is a calcified patch to be seen in the skiagram. However, the surgical approach for the two lesions is in most cases identical.

The varieties of symptoms produced by a cerebral aneurysm are well known, and I have only referred to the condition here because I have seen two or three cases, originally diagnosed as pituitary tumour, which proved on investigation to be almost certainly cases of cerebral aneurysm. Cerebral aneurysm may occasionally produce optic atrophy and bitemporal hemianopsia, and it is very important for the neurological surgeon to be aware of the condition, lest he should open an aneurysm in mistake for a cyst, and thus have a death on the operating table.

All the lesions which I have mentioned so far, have been situated in the region of the sella turcica, but another type of case in which a diagnosis of pituitary disease is often made is one in which the sella turcica has become enlarged as a result of secondary hydrocephalus. A tumour that produces hydrocephalus as, for example, a tumour of the vermis, causes great enlargement of the third ventricle, which presses down on to the diaphragma sellæ and so leads to enlargement of the sella turcica.

I have dealt with the problems in diagnosis that may confront the surgeon, but much more important problems in the diagnosis of pituitary disease fall to the lot of the ophthalmologist. In by far the greatest number of cases of pituitary tumour the patients complain first of failing vision. For the ophthalmologist the diagnosis is not difficult if he examines the visual fields. In most of the cases in which the correct diagnosis has not been made until vision has been grossly damaged, investigation of the visual fields has been neglected. One sees certain patients who have had courses of antisyphilitic treatment on account of optic atrophy, or have had nasal operations performed. These mistakes would not occur

if it was considered essential to examine the visual fields in all cases of failing vision for which no local causes can be found.

**Dr. F. A. Pickworth** showed a large number of slides illustrating the relationship of infection in the sphenoidal sinus to disorders of the pituitary gland and adjacent brain substance, in the subjects of mental disorder. His thesis was that the relationship of post-nasal sepsis to disorders of the pituitary gland had been somewhat neglected, and that a large number of patients in mental hospitals showed symptoms of endocrine dysfunction, which could be correlated by histological methods, with involvement of the pituitary gland by the sphenoidal sinus infections also common in such patients.

**Mr. T. C. Graves** said that the occurrence of endocrine disturbances in patients suffering from mental disorders was a generally accepted fact, but these disturbances were so complex, so variable and so often overshadowed by the mental symptoms, that they might not be adequately recognized. This was especially the case in pituitary disease, the symptoms of which were indefinite—varying, as they did, according to the extent of disturbance of function of adjacent nervous tissue.

Certain symptoms, however, frequently seen in the subjects of mental disorder, appeared to have a direct relation to pituitary function. These were: (1) General loss of muscle tone; (2) disturbance of the peripheral circulation, causing extreme facial pallor and cyanosis of dependent parts; (3) disturbance of nutrition, emaciation which might be followed by obesity; (4) disturbances of the reproductive mechanism (e.g. amenorrhœa).

Several other symptoms were of value as indirect evidence of pituitary disease since they were referable to that part of the brain adjacent to the pituitary stalk. For instance, absence of pyrexial response to the injection of substances which produced a high temperature in normal persons. In these cases the usual increase in pulse-rate occurred, as in normal individuals.

[Mr. Graves recorded in detail two cases illustrating these observations.]

**Dr. Adie** (in reply) said he had no criticism to offer on Mr. Dott's perfect demonstration, but he did not like the expression "cranio-pharyngioma," and he did not think putting the suffix "oma" on to the situation in which a tumour grew was a very good practice, e.g., meningioma.

He wished that he had Professor Dodds to work on the cases at Queen Square Hospital. Those engaged in that hospital would now work more closely with the biochemist.

Mr. Cairns had done much good service in pointing out that not all fat boys were suffering from pituitary tumour. If a fat boy with small genitalia presented himself in the out-patient department and the students were asked to diagnose the condition they at once said "pituitary tumour." Fortunately, in most cases that diagnosis was not correct.

He agreed that some gauge was required to measure the increase or reduction in the size of patients' hands, and suggested that the wedding ring, or a graduated series of rings, might be a good guide.

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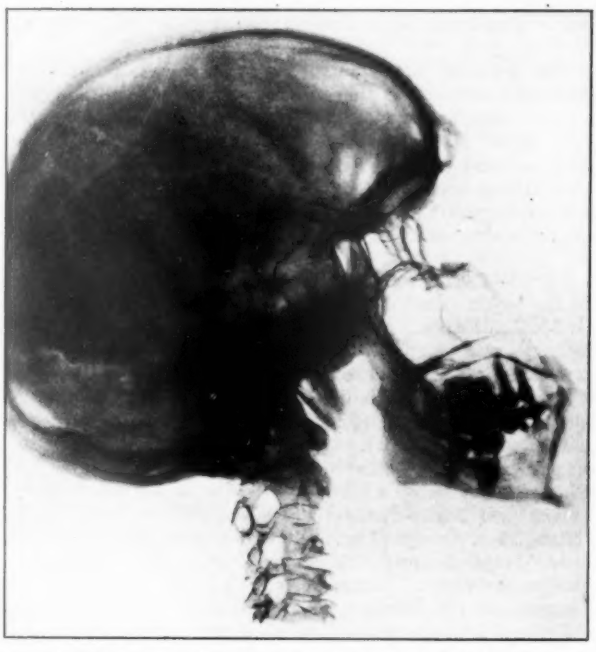
CASES SHOWN AT THE CLINICAL MEETING HELD AT THE LONDON HOSPITAL, E.1, NOVEMBER 26, 1929.

**Pituitary Tumour.**—R. A. ROWLANDS, M.D., and S. LEVY SIMPSON, M.R.C.P. —Patient, male, aged 35, admitted to hospital October 20, 1929. Quite well until eight years ago (1920), then had pneumonia and pleurisy. He recovered without obvious complications, but has never been well since. Has frequent colds and influenza and feels languid and weak. Feels the cold intensely in spite of much

additional clothing. Hands and feet often cold and numb. Skin has become smooth and dry, and the skin of the legs exfoliates, fine scales falling out of his garments to the floor. Sometimes experiences sensation of "hot sweats," followed by cold shivers, giddiness and blurred vision, but has never become unconscious. Apart from these attacks, his vision has not troubled him. Headaches not a prominent symptom, but occur sometimes as severe ache across frontal region, and on vertex; not associated with nausea or vomiting, Occasionally sensation of "hot sweats" is limited to head. Facial hair does not grow so quickly as formerly. Patient now shaves only once a week instead of daily; has noticed loss of pubic and axillary hair. His face has become much paler and he believes that his general appearance has changed.

Patient is not impotent, but during the last few years no emission has ever taken place. He believes his genitals have decreased in size. Sphincters not impaired.



Case of pituitary tumour (Dr. R. A. Rowlands and Dr. S. Levy Simpson).

No increase in weight. Patient is fairly well nourished, but there is no marked adiposity.

The facial appearance is suggestive of a myxœdematous condition. Skin thick, dry and pallid. Hardly any hair present over face. Pubic hair also scanty and of feminine distribution; axillary hair almost absent. Fingers rather long and tapering towards the extremities. Genital organs smaller than the average. Hands are cold to touch and bodily temperature is persistently subnormal (97° F.). Respiration does not exceed 20. Pulse about 66. Mental condition normal.

Visual fields, to rough test and as measured by the perimeter, are quite full. Right disc normal; left, pale with a deep physiological cup. No gross impairment of vision.

Remainder of central nervous system normal. Lungs and heart normal. Blood-pressure 110/70. Liver, spleen not enlarged.

Blood-count (October 20 1929), showed nothing abnormal, except a slight relative lymphocytosis.

Erythrocytes 5,000,000, hæmoglobin 72%, colour-index 0·72. Leucocytes 6,640 (*Differential count*: Polymorphonuclear neutrophils 51%, small lymphocytes 38%, large lymphocytes 7%, large hyaline 3%, coarsely granular basophils 1%).

While in hospital there was a slight transient glycosuria.

Carbohydrate tolerance tests gave a curve which approximated to the "lag-type," but there was no resulting glycosuria.

10.30 a.m., fasting level, 0·062%; 1.15 a.m., blood sugar, 0·207%; 12.30 p.m., blood sugar, 0·077%.

Skiagram of skull shows enlargement of the pituitary fossa. The floor of the fossa appears to dip into the sphenoid sinus. The posterior clinoid processes are long and eroded. The radiological finding agrees with the diagnosis of pituitary tumour.

*Comment.*—The tumour is probably a chromophobe adenoma of the anterior pituitary. Headaches are not very severe or persistent in this particular case, but recently there have been attacks of pain referred to the first division of the fifth nerve on the left side. This sometimes occurs with pituitary tumours, owing to pressure on the fifth nerve or one of its branches. The fields of vision are normal, and the fundi are almost normal, there being very slight pallor of the left disc. In view of these findings and the state of hypopituitarism, it might be advisable to postpone operative interference.

**Chronic Lymphatic Leukæmia with Aleukæmic Phase.** — R. A. ROWLANDS, M.D., and S. LEVY SIMPSON, M.R.C.P.: With a Note on Lymphosarcoma, by H. M. TURNBULL, D.M.—Patient, female, aged 59, married, first came to the out-patient department on January 10, 1928, complaining of "glands in the neck," dyspnœa on exertion and general lassitude. Patient had had one child who had died from pneumonia. No history of miscarriages or stillbirths. Apart from rheumatic fever when aged 17, and vague transitory paresis of the right hand, had been comparatively well until early in 1927, when she had a slight sore throat, and noticed swollen glands on both sides of neck. Some months later had dyspnœa on exertion and general lassitude.

*Condition when first seen.*—Several enlarged glands were present in the anterior and posterior triangles of the neck on both sides, and some smaller glands in both axillæ and groins. No evidence at that time of enlargement of spleen or liver. A few dilated veins on the chest. Lungs normal; no evidence of pressure on bronchi. No hæmic murmurs in the heart. Blood-pressure 120/80; arteries showed no abnormality. Central nervous system normal. No pallor of mucous membranes. The blood-count at that time was: Erythrocytes 4,700,000, hæmoglobin 70%, colour-index 0·74, leucocytes 8,200. Differential count showed 46% polymorphonuclear neutrophils, 4% eosinophils, 46% small lymphocytes, 2% large lymphocytes, 2% large hyaline cells.

The patient was at that time unwilling to come into hospital for biopsy of a gland, and a tentative diagnosis of chronic lymphatic aleukæmic leukæmia was made.

| 1928 | Total leucocytes | Small lymphocytes |
|---|---|---|
| February 21 | 6,200 | 37% |
| July 24 | 8,240 | 60% |
| October 16 | 10,680 | 52% |

There was then apparently a period of non-attendance. On May 14, 1929, total leucocytes had increased to 34,000, small lymphocytes being 51%. The glands in the meantime had increased considerably in size, and the patient consented to

enter hospital on August 27, 1929. The languor and dyspnœa had also become more troublesome.

*Condition on Examination.*—Patient looked wasted and ill. Gross deformity of the neck owing to large masses of diffluent glands on both sides. Large glands in axillæ and groins. Spleen just palpable on deep inspiration. Liver slightly enlarged.

September 2, 1929.—A small gland was removed from the posterior triangle of the neck, under local anæsthetic.

*Pathological Report by Professor H. M. Turnbull.* (*S.D.* 2037. 1929.)

The capsule is not included in the section, so that the condition of the periadenoid tissue is not shown. Lymphatic sinuses are not recognizable and there are no "germ centres." The gland is evenly infiltrated with lymphocytes, amongst which are a few large mononuclear reticulum cells. There are no large blood-vessels in the section. Most of the small vessels contain several lymphocytes similar to those in the adenoid tissue, and there are very few leucocytes in vessels. But the actual number of lymphocytes in the vessels is not sufficiently great to make certain a diagnosis of lymphadenoid leukæmia. The diagnosis lies between the so-called "lymphosarcomatosis" and lymphadenoid leukæmia.

The blood-count on admission, August 27, 1929, showed 65,280 leucocytes, 86% lymphocytes. There was slight poikilocytosis and anisocytosis.

Blood-count, September 11, 1929.—Erythrocytes 3,500,000, hæmoglobin 55%, colour-index 0·72, leucocytes 70,680.

The differential count showed polymorphonuclear neutrophils 6·4%, small lymphocytes 87%, large lymphocytes 6%, transitional neutrophils 0·6%. Two megaloblasts were seen in counting 500 white cells.

September 20, 1929.—Dr. G. Vilvandré began X-ray treatment to the right side of the neck and both axillæ. This was repeated on September 27.

Radiograms of both femora showed alteration of texture, of a character not infrequently seen in chronic lymphatic leukæmia (Dr. S. G. Scott). Radiogram of hands showed slight rarefaction. Radius and ulna, and tibiæ, normal.

Patient was unwilling to remain in hospital and left on September 30 with a view to attending as an out-patient.

She was again seen, however, four days later (October 3, 1929) complaining of dyspnœa, and there were then signs of a pleural effusion on the right side.

The next day, 6 c.c. of turbid yellow blood-stained pleural effusion were removed for cytological examination, which showed small lymphocytes 95%, finely granular oxyphils 3%, endothelial cells 2%. The culture was sterile.

On October 9, 1929, 30 ounces of fluid were removed, and a week later a similar quantity was withdrawn from the left side of the chest. After some days the fluid began to reaccumulate.

*Blood-count*, October 31, 1929.—Total number of leucocytes reduced to 18,000, with 76% small lymphocytes. On November 6 the blood-count had hardly altered (18,040 leucocytes, 70% small lymphocytes). The glands in the neck and axillæ have decreased considerably in size subsequent to the X-ray treatment.

(We are indebted to Dr. P. N. Panton for reports on the blood-counts and pleural fluid.)

*Comment.*—A point of interest is the aleukæmic phase of nine months during which period the patient was under observation and several blood-counts were made. The ultimate picture was identical with a chronic lymphatic leukæmia. Microscopical examination of a gland did not permit differentiation between lymphosarcomatosis or lymphadenoid leukæmia.

The term chronic lymphatic aleukæmic leukæmia might perhaps be replaced by aleukæmic lymphadenosis. The relative lymphocytosis suggested the tentative diagnosis.

Many discussions on the differential diagnosis of aleukæmic leukæmia and lymphosarcomatosis are hampered by lack of definition.

The term pseudo-leukæmia was first used by Cohnheim [1] in 1865. He described the case of a man, aged 24, who had a three months' history of epistaxis, malaise and weakness. The total cells were less than normal, but the proportion of whites to reds was normal. At autopsy the organs showed the changes of lymphatic leukæmia.

Subsequent to Cohnheim's paper many conditions were included under the term pseudo-leukæmia, and pathologists spent the next twenty years separating off tuberculosis, Hodgkin's granuloma and allied conditions, from what had become a heterogeneous group.

In 1899, Turk [2] put forward evidence showing that pseudo-leukæmia was merely a phase of leukæmia.

Turk's view was supported by Klein [3] in 1903, and Sternberg [4] 1912. Ewing [5] 1928 was not inclined to agree.

The term lymphosarcomatosis was used by Professor Kundrat [6] in 1893 to describe a condition which he thought was related to pseudo-leukæmia and granuloma malignum and which could develop from them. (The term granuloma malignum is probably used here as a synonym for Hodgkin's granuloma.)

Apart from the heading "lympho-sarkomatosis," Kundrat uses the term "lympho-sarkom" throughout his paper. He stressed the point that lympho-sarkom arises from groups of glands or follicles, never from a single gland or follicle (thus presumably showing their resemblance to the pseudo-leukæmias and granulomas).

Lympho-sarkom (Kundrat stated) commences as a general hyperplasia of the lymph glands, but sooner or later it overruns or breaks through the capsule of the glands and infiltrates the surrounding tissue. The invasion proceeds more malignantly than any carcinoma or sarcoma, and Kundrat suggests that this fact divides it from the leukæmias. A criterion which cannot, we think, be accepted as an absolute differentiation.

Remote lesions in lympho-sarkom are not true metastases, according to Kundrat, as they could be traced through lymphatic spread. Blood-metastases Kundrat consider to be very rare. Thus the lympho-sarkom differed from other sarcomata. Kundrat observed that it was remarkable that such a penetrating tumour as lympho-sarkom should not break into blood-channels and have blood-metastases.

In further differentiation from the leukæmias, Kundrat stated that in lympho-sarkom the diffuse infiltrations of the liver and the spleen, and the numerous nodule-shaped metastases never occurred. In the lympho-sarkom of Kundrat the liver and spleen were not enlarged and more frequently were small. The bone-marrow also showed no peculiar changes.

In 1904, Yamasaki [7] pointed out that lymphosarcoma may arise as a terminal stage in Hodgkin's disease.

In 1910, Welch [8] published a case in which a cervical gland removed six months before death showed Hodgkin's granuloma, while the tumours removed at autopsy from the neck, dura mater, liver, and lung, showed large round-cell sarcoma.

Another condition should be mentioned, namely, the leucosarcomatoses of Sternberg [9], 1908. Sternberg regards them as a combination of lymphatic leukæmia and lymphosarcomatosis. The chloromas he considered belong to this group.

Although there were usually no gross blood changes in lymphosarcomatosis, it must be admitted that various blood changes have been described with lympho-sarcomatosis. Many records are unreliable because of the different pathological conceptions.

LYMPHOSARCOMA. BY H. M. TURNBULL, D.M.

I define "lymphosarcoma" as a condition in which cells resembling large or small lymphocytes or lymphoblasts lie in the meshes of a fibrillar reticulum, and by substituting this structure for that normally seen in adenoid and other tissues give the general impression of an infiltrative neoplasm. The condition commences in adenoid tissue. It may affect a

single group of lymphatic glands. Usually it affects several areas of adenoid tissue. Thus in the intestines there are almost invariably two or three widely separated foci, or more commonly the lymph follicles throughout the greater part of the stomach and intestines appear to be affected simultaneously. The condition usually extends extensively into the periadenoid tissue. Thus in the intestine the affected follicles become enlarged, and then the wall of the gut becomes widely replaced by infiltration. At the same time the regional lymphatic glands are almost invariably infiltrated and their normal structure obscured. In many cases the primary focus is in the mediastinal glands; then, all the glands and periadenoid tissue frequently form a single mass of infiltration. There are occasionally secondary foci in positions in which adenoid tissue is not normally present, for instance in the skin, the kidney, the uterus or the testicle. Usually the secondaries affect organs in which adenoid tissue is present—the spleen, the marrow and the portal systems of the liver. In many cases these three organs are not affected. When the spleen is affected cells multiply in the centres of Malpighian bodies; the affected Malpighian bodies then become enlarged; in some examples all the Malpighian bodies are greatly enlarged and have coalesced to form a network which encloses small areas of pulp. In the latter examples the spleen is greatly enlarged. In the liver an extension of the infiltration from portal systems may lead to the formation of large nodules. Infiltration of the marrow tends to be nodular or patchy, and less uniform than the infiltrations of the leukæmias. In most, though not all, of the examples in which the spleen and marrow are affected the condition is widespread throughout the body. Characteristically in such cases all the lymphatic glands, the adenoid tissue throughout the greater part of the stomach and intestine, and the liver are implicated in addition to the spleen and marrow, whilst other areas of infiltration are usually present in the skin, myocardium or elsewhere. To these examples of wide dissemination the term "lymphosarcomatosis" can be justly applied.

When a single gland is alone available for examination it is impossible to differentiate the condition with certainty from lymphadenoid leukæmia or pseudo-leukæmia—the latter term being employed to denote a condition in which the organs are histologically similar to the organs in leukæmia, but the blood is not leukæmic. The presence of numerous lymphocytes of the same form within the vessels in the section does not exclude lymphosarcomatosis, because a lymphadenoid leukæmia may appear in the late stages of that condition. Periadenoid infiltration occurs in lymphadenoid leukæmia, and, as in myeloid leukæmia, may lead to a massive tumour-like infiltration. At necropsy a diagnosis of lymphosarcoma is not justified by the presence of nodular infiltrations in tissues which are not adenoid and have no special myelogenous potentiality. Such infiltrations may occur in the leukæmias. Thus, in a recent example of clinically and anatomically typical lymphadenoid leukæmia an infiltration of the prostate was conspicuous to the naked eye. The one organ by which a differential diagnosis can be made with certainty is the spleen. If the spleen is unaffected leukæmia is excluded. If the spleen is affected the infiltration differs conspicuously from that in the leukæmia. As already described lymphosarcoma commences within, and is confined to, the Malpighian bodies in the spleen. In lymphadenoid leukæmia I have found no evidence that the infiltration commences in the Malpighian bodies. I believe that in lymphadenoid leukæmia, as in myeloid leukæmia, the infiltration affects the pulp primarily. At any rate, in the earliest examples of lymphadenoid leukæmia that I have examined the spleen has been evenly infiltrated throughout, and the site of Malpighian bodies could only be recognized by the special arrangement of the reticulum.

The lymphosarcomas as defined above do not appear to be neoplasms in the restricted sense. In lymphosarcoma adenoid nodules are affected successively or simultaneously; no ordinary sarcoma picks out homologous sites for secondaries in this way. Further, the histological changes in early secondaries in the adenoid nodules in the intestine or in the Malpighian bodies of the spleen, and the histological changes in lymphatic glands in an early stage of implication, are those of a reaction *in situ* and not of a metastasis. The condition is a lymphogranuloma rather than a neoplasm, and is closely allied to Hodgkin's lymphogranuloma. In examples of Hodgkin's disease, in which some of the lesions are characteristic, there may be other lesions, the so-called sarcomatous, which cannot be differentiated from lymphosarcoma. In some examples of lymphosarcoma there may be a proliferation of reticulum cells and an infiltration with plasma cells, and a few eosinophil leucocytes, although the characteristic picture of Hodgkin's granuloma is nowhere found. Every time that I examine my index cards of lymphosarcoma more examples are tentatively transferred to those of Hodgkin's lymphogranuloma! The only difficulty in regarding as aberrant forms

of Hodgkin's lymphogranuloma all the lymphosarcomata, at any rate all in which the spleen is implicated, is to explain why the adenoid tissue of the intestine should so seldom be affected when the typical reaction of Hodgkin's granuloma is found in some portions of the cadaver, whilst the adenoid tissue of the intestine should so very frequently be affected when the typical reaction of Hodgkin's granuloma is found in no section of a complete series.

Professor Turnbull includes a group without changes in the spleen, liver and bone-marrow, which would appear to correspond to Kundrat's group. Professor Turnbull has pointed out, however, that in many cases the spleen, liver, and marrow are affected. The changes in the spleen are the key to the differential diagnosis from the leukæmic group, in that, with lymphosarcomatosis, the changes are limited to the Malpighian bodies, there being no diffuse involvement of the pulp as in leukæmias. The group of lymphosarcomatosis with changes in the spleen may approximate closely to Hodgkin's granuloma.

From the point of view of attempted differential diagnosis during life, it is important to realize that microscopical examination of a gland does not permit the differentiation of lymphosarcomatosis and aleukæmic leukæmia. It may be impossible to speak with any certainty before a complete autopsy has been performed. The further elucidation of these problems would be aided by a more dynamic conception of the conditions, with periodic biopsy of glands, a correlated series of blood-counts, and an ultimate complete autopsy.

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**(3) Hypercholesterinæmia.**—W. RUSSELL BRAIN, D.M., and F. B. BYROM, M.D.—*History of Present Illness.*—F. M., married woman, aged 33, admitted to London Hospital, June 5, 1929. Complained of flatulence and nausea of six months' duration. For four months skin had been yellow, stools pale and urine dark. At this time raised yellow spots appeared around the eyes, and later on the face, forearms, and hands.

*Previous History.*—Nine years previously, abscess of breast, four years previously brief illness said to have been "inflammation of the kidneys and bladder." Husband died two and a half years ago from pulmonary tuberculosis. Has had four children, two of whom are now alive.

*Condition on Admission.*—Rather wasted woman with deep jaundice and generalized dusky pigmentation. Confluent papular xanthomata thickly scattered over face, breast and neck and (especially) on the palms and antecubital fossæ. The creases of the palms were studded with rows of raised xanthomata, which hindered patient from gripping hard objects.

*Abdomen.*—Liver enlarged almost down to umbilicus; surface smooth, hard and not tender. Spleen was palpable, extending downwards for about two fingers'-breadth below the costal margin. The urine contained much bile pigment, and a cloud of albumin.

*Exploratory Laparotomy* (June 26, 1929, by Mr. A. J. Walton).—Liver uniformly and diffusely enlarged; gall-bladder and bile ducts normal. The spleen, which was considerably enlarged, was removed.

*Subsequent Progress.*—The jaundice has persisted since the operation. The xanthomata became paler and less prominent for a few weeks, but have since steadily increased in size and extent. The liver has gradually increased in size and now reaches to the right iliac fossa. The general condition of the patient has remained remarkably good.

*Blood-count* (before operation).—Red corpuscles 4,800,000, colour-index 0·8, leucocytes 4,580. Three weeks after operation: Red corpuscles 4,600,000, colour-index 0·68, leucocytes 12,480.

*Fragility of Red Corpuscles.*—June 26, 1929, normal.

*Blood-platelets* (after operation).—July 2, 1,500,000 per c.mm.; July 15, 270,000 per c.mm.

*Van den Bergh Reaction.*—June 24, strong biphasic reaction, 5 mgm. bilirubin per 100 c.c.; July 15, 2·5 mgm.; August 9, 4·5 mgm.; October 4, 5 mgm.; November 1, 3·75 mgm.

*Plasma Cholesterol and Lecithin* (expressed as ether soluble phosphorus):—

| | Cholesterol | Lecithin |
|---|---|---|
| June 25 | 800 mgm. % | 79 mgm. % |
| June 29 | 600 ,, | 55 ,, |
| July 3 | 430 ,, | 50 ,, |
| July 10 | 440 ,, | 45 ,, |
| July 15 | 400 ,, | 60 ,, |
| August 9 | 670 ,, | 76 ,, |
| September 2 | 670 ,, | 86 ,, |
| October 4 | 670 ,, | 90 ,, |

*Wassermann reaction* negative. *Blood-sugar* 0·117%; *Blood-urea* 0·034%.

*Cerebrospinal fluid.*—No cells seen. Protein 0·02%. Wassermann reaction negative. *Diastatic index* 10°.

*Pathological Report by Professor H. M. Turnbull.*

*Spleen and Lymph-glands from F.M.* (*S.D.* 1426. 1929.)

Macroscopic.—*The spleen* weighed 15¾ oz. and measured 15 by 10·5 by 5·5 cm. The veins in the hilum had transparent walls and a smooth lining; the splenic arteries had a smooth lining. The largest vein measured 2 cm. in circumference, the largest artery 0·8 cm. The capsule had been torn from the upper two-thirds of the postero-mesial border; the remainder of the capsule was covered with delicate fibrous tags. The spleen was pliable and felt doughy. On section the Malpighian bodies projected from a flat-cut surface as conspicuous, greyish-white, glistening nodules, which measured up to 0·2 cm. in diameter. The pulp was pinkish-red, tinged faintly with brown. Repeated sections revealed neither punctiform hæmorrhages nor rusty spots.

In the hilum were a few *hilar lymphatic glands*, of which the largest measured 2 by 0·8 by 0·5 cm. The glands were soft and showed brownish cut surfaces.

An *hepatic gland* in formaldehyde solution accompanied the specimen. It measured 2·3 by 1·8 by 1 cm. Cut surfaces were flat, and showed dull grey dots and streaks in a faintly yellow ground.

Microscopic.—Portions were taken for microscopic examination from the spleen, a hilar gland, and the hepatic gland, and were fixed in 4% buffered saline formaldehyde, Zenker's solution and absolute alcohol.

(1) *Spleen.*—The Malpighian bodies are large, and have conspicuous pale centres, in which are reticulum cells, with abundant ill-defined vesiculated cytoplasm, numerous large lymphocytes, some showing karyokinesis, and a considerable number of small lymphocytes. In the peripheries of the body are many neutrophil leucocytes. The media of the arteries and arterioles is swollen, and forms a thick ring of vesiculated tissue containing very pale concentric nuclei; some nuclei can only just be recognized. The endothelial cells are less swollen and their nuclei are deeply stained. The lumen is narrowed. In the arterioles the swelling is very great, the lumen is completely or almost completely occluded, and the endothelial lining is usually lost. Consequently in cross section the arterioles appear as conspicuous spheres containing two or three concentric rows of nuclei. The arterial capillaries show similar changes, but the nuclei form a single ring. There are numerous plasma cells in the adenoid adventitia of the arteries, and still more in that of the arterioles. Plasma cells also surround the veins on their entry into trabeculæ. The bodies of the reticulum cells in the strands of the pulp are rarely defined, the nuclei usually lying in a common vesiculated ground. The fibrils of the reticulum are demonstrated by Laidlaw's silver impregnation, but only an occasional, feebly stained fibril is shown by van Gieson's mixture. Within the pulp strands in places there are numerous neutrophil leucocytes, but

usually there are only occasional plasma cells, lymphocytes, neutrophil and eosinophil leucocytes, or red corpuscles. There are one or two phagocytes containing red corpuscles. The venous capillaries are well defined; their endothelium is swollen; their lumina contain numerous neutrophil leucocytes, many large mononuclear leucocytes and eosinophil leucocytes, relatively few lymphocytes and occasional cells resembling the swollen endothelium.

In Herxheimer preparations fat granules are confined to a few spindle fibrocytes in trabeculæ. No doubly refractile substance is demonstrated by the polariscope. No substance is stained by the Weigert-Pal method. Very few granules of iron were found on searching sections of tissue, which, after fixation either in alcohol or in formaldehyde, had been stained by the Prussian blue method reinforced by heat.

(2) *Splenic and* (3) *Hepatic Lymph Glands.*—Some of the cortical nodules contain pale centres similar to those in the spleen. The lymphatic sinuses contain a large number of free round endothelial cells, of which a few contain ingested red corpuscles. Amongst the free endothelial cells are small lymphocytes. There are a few large lymphocytes containing karyokinetic figures in the medullary strands.

No fat is demonstrated by Herxheimer's method, and no iron by the Prussian blue method reinforced by heat.

*Remarks.*—The appearances in the spleen are those of a subacute inflammation, with a remarkable degeneration of the walls of the arterioles and arterial capillaries. The lymphatic glands show sinus-catarrh.

Dr. F. PARKES WEBER said that he had been obliged to alter his view in regard to some of these cases of hypercholesterinæmia with chronic jaundice, xanthomatosis (especially "sheet-like" cutaneous xanthoma of the neck), and splenomegaly. In some cases he thought that the primary factor was a constitutional metabolic abnormality, giving rise to hypercholesterinæmia, which in its turn led to xanthomatosis of biliary ducts, giving rise to more or less obstructive jaundice, still higher hypercholesterinæmia, increased cutaneous xanthomatosis, and a kind of "lipoid splenomegaly" (S. C. Dyke).[1]

**Gaucher's Disease Thirteen Years after Splenectomy.**—DONALD HUNTER, M.D., and WILLIAM EVANS, M.D.—I. W., married woman, aged 60.

*History.*—Pigmentation of the face evidently present in childhood, for at age of 8 her school teacher used to say to her, "Go out at once and wash yourself, you dirty girl."

At the age of 10, several attacks of severe epistaxis. Catamenia commenced at the age of 13, and from the onset the loss appears to have been excessive. Attacks of severe epistaxis occurred at the ages of 26 and 27. Two years later patient noticed a lump in the left hypochondrium and began to have periodic attacks of pain in this region.

At the age of 30 the lump had increased in size and caused the abdomen to swell. Patient was admitted to St. George's Hospital, where treatment by medicine is alleged by the patient to have "dispersed the lump." (Her case-notes for that time are not available.) For a period of six years, between the ages of 32 and 38, the patient suffered from severe menorrhagia and metrorrhagia, and later bleeding occurred from the gums and lasted for nine months. At this time she was treated by her doctor with raw meat and red wine because of anæmia. At the age of 46 she suffered from several attacks of slight hæmoptysis. Menopause occurred at the age of 47. She then experienced a return of the abdominal pain and the lump reappeared.

In December, 1916, the patient was admitted to the London Hospital under the care of Dr. Theodore Thompson. The spleen was found to reach 2 in. below the level of the umbilicus. The edge of the liver was felt about 2 in. below the right costal margin. There was no enlargement of lymphatic glands.

In January, 1917, splenectomy was performed by Mr. Sherren. Adhesions were found to the diaphragm and parietal peritoneum. The liver was slightly enlarged but showed no evidence of fibrosis. There was no free fluid in the peritoneal cavity.

[1] In a previous discussion Dr. Weber had advised a trial of therapeutic gall-bladder fistula in some cases, when operatively feasible. This might break the vicious circle.

*Progress.*—The patient has had no pain since the operation. She states that the face and arms have become much less brown. During the last twelve months she has complained of noises in the ears, bitemporal headache following needlework or reading, and occasional attacks of hæmoptysis. She has never suffered from hæmatemesis, melæna nor hæmaturia.

*On Examination.*—A short, well-nourished woman. Weight, 6 st. 13 lb. No pigmentation of mucous membranes. Pigmentation of face and arms, of a deep brown-yellow colour, rather like sunburn, with darker mottling of forearms. Skin fine in texture and slightly glossy. Axillary hair absent, pubic hair scanty, hair of scalp normal. No pigmented scars and no purpura. No clinical evidence of jaundice. Localized triangular deposits of fat (pingueculæ) in conjunctiva between left inner canthus and cornea and between right outer canthus and cornea. Radial and brachial arteries firm and slightly tortuous. Blood-pressure 205/110. The apex-beat is forcible but not displaced. The first sound at the apex is loud; the aortic second sound is not accentuated. Examination of the fundi reveals tortuous arteries nipping the veins. No abnormal physical signs in lungs or nervous system. No abnormal veins on abdominal wall or elsewhere on trunk. No pigmentation of scar of left upper paramedian incision. Firm edge of liver palpable 2 in. below right costal margin. No enlargement of lymphatic glands. No œdema of feet. No swelling of joints. No deformity, tenderness, nor swellings of bones. Urine shows cloud of albumin, no casts, no bile-pigment, and no excess of urobilinogen.

*Special Tests.*—Wassermann reaction negative. Fragility of red blood-corpuscles normal. Plasma cholesterol 0·103 per cent. Radiograms of bones show no abnormality.

| Date | Red blood-cells per c.mm. | Hæmoglobin % | Colour-index | Leucocytes per c.mm. | Polymorphonuclears % | Lymphocytes % | Platelets per c.mm. | Van den Bergh's reaction |
|---|---|---|---|---|---|---|---|---|
| 2.1.17 | 4,480,000 | 85 | 0·9 | 2,600 | 42 | 50 | — | — |
| *12.1.17—Splenectomy* | | | | | | | | |
| 24.1.17 | 4,283,000 | 75 | 0·9 | 12,200 | 72·5 | 19 | — | — |
| 16.7.28 | 4,700,000 | 49 | 0·52 | 4,440 | 41 | 52 | — | direct, negative; indirect, 1·56 mgm. per 100 c.c. |
| 27.3.29 | 4,400,000 | 63 | 0·71 | 8,280 | 40 | 53 | 110,000 | — |
| | 1 normoblast in 200 white cells | | | | | | | |
| 5.11.29 | 3,900,000 | 67 | 0·87 | 8,480 | 65 | 32 | 120,000 | direct, negative; indirect, 1·25 mgm. per 100 c.c. |

*Family History.*—Sister (M. J. J.), aged 60, died from "cerebral thrombosis" in Whipps Cross Hospital, in January, 1927. She had a large spleen but refused operation. Her skin was always fair and clear. She was never jaundiced and there was no history of hæmorrhages. She was married but had no children. Daughter (F. M. W.), aged 28. Examined in May, 1927, at the London Hospital. No splenomegaly. Fragility of red cells normal. Son (F. W.W.), aged 27. Serving with Army abroad. Fit and strong.

Patient's brother (F. H.), aged 57, suffers from indigestion. Has three healthy sons. Another brother (F. H.), aged 66, is well and has no family.

Patient had three miscarriages, all at eight weeks, "on account of spleen."

*Pathological Report by Professor H. M. Turnbull.*

*Spleen from I. W., aged* 47. (*S.D.* 48. 1917.)

Macroscopic: The spleen weighed 1 lb. 8 oz. On the surface were a few fibrous tags. The intima of the largest of three arteries in the hilum showed very faint, fatty powdering; the other arteries and veins appeared to be normal. Nodules averaging 0·4 cm. in diameter, the largest being 1·7 cm. in diameter and 0·3 cm. high, raised the capsule all over the outer surface. On section the largest nodule showed numerous yellow and purple dots and streaks in a ground of red darker than that of the rest of the pulp. The rest of the pulp was dark

red beset with closely-packed very small white specks; amongst these were trabeculæ, which could be distinguished as narrow streaks, pin-head purple hæmorrhages, and several yellow calcareous nodules, of which the largest measured 0·4 cm. in diameter.

Microscopic: Sections were taken to include the nodules projecting upon the surface and the hæmorrhages in the pulp.

The Malpighian bodies are few and small; in the subcapsular nodules they are reduced to a few small remnants. The pulp is occupied by numerous round and oval acinar masses of large cells. In the subcapsular nodules these masses are exceptionally large and occupy almost the whole of the pulp. Almost all the large cells have a diameter four times as great as that of a red corpuscle, but many are much larger; there are many multinuclear giant forms. The cells are polygonal with rounded corners, or spherical. The cytoplasm shows a reticulum enclosing vacuoles which are usually small but sometimes large. The nucleus is relatively small, having a diameter equal to a quarter or a third of that of the cell. It is round, oval, or more often crenated. The structure resembles that of the nuclei of the endothelial cells of the venous capillaries except that the nucleoplasm is usually very deeply stained. Pyknosis is frequent; karyorrhexis and karyolysis are less common, although many cells have lost their nuclei. The multinuclear giant-cells are only slightly larger than the larger mononuclear cells. Six nuclei are frequently present. They are irregularly placed, but tend to lie in peripheral planes. They are often distorted and pyknotic.

The cytoplasm is tinted brown by Herxheimer's scarlet red but no fatty substance is demonstrated by this stain, the Smith-Dietrich method, or the polariscope.

Laidlaw's silver impregnation shows occasional reticular fibrils within most of the cellular masses, so that these masses clearly occupy the reticular strands of the pulp. Other masses appear to distend venous capillaries, particularly in the subcapsular nodules; there appear, indeed, to be transition forms between the large cells and endothelial cells lining venous capillaries. But this has not yet been proved, because in the sections stained so far to demonstrate elastic fibres the elastic rings in the walls of the venous capillaries have not been stained.

Amongst the large cells is a variable number of red corpuscles, eosinophil leucocytes and, less numerous, neutrophil leucocytes and lymphocytes. In the subcapsular nodules there are patchy, fibrotic areas in which the fibrils of the reticulum are increased in number, are stained deep red by van Gieson's method, and enclose only a few of the large cells and a few lymphocytes and plasma cells. The pulp strands that are not occupied by the large cells contain lymphocytes, free reticulum cells, red corpuscles, plasma cells and eosinophil leucocytes. The hæmorrhages are into and about the sheaths of arteries just before they reach Malpighian bodies; there is one iron-pigmented scar in a similar position.

*Remarks.*—The condition of the spleen is typical of Gaucher's disease. Professor Mandelbaum asked for sections, and confirmed this diagnosis in his acknowledgment.

*Comment.*—Gaucher's disease is rare, and the patient described here is the only authentic case admitted to the London Hospital. The condition was first described in 1882 by Gaucher [1] who believed that it was a "primary epithelioma" of the spleen. Bovaird [2], in 1900, described the changes in the liver as well as in the spleen, and drew attention to the familial incidence of the disease. Mandlebaum and Downey [3], in 1916, were the first to suggest that the disease was fundamentally a disturbance of metabolism. Lieb [4] and others [5], [6], [7] have since produced evidence that the Gaucher substance is "kerasin—a galacto-lipin."

Brill [8] in 1904 was the first to draw attention to the presence of Gaucher cells in the bone-marrow. In 1922, Pick [9] discovered a gross osseous form of the disease. He described cases with marked skeletal changes in the form of erosion of the corticalis, pathological fractures, and angular curvature of the spine. Junghagen [10], in 1926, called attention to the use of radiograms of bones in the diagnosis of Gaucher's splenomegaly. In every case of splenomegaly of obscure origin it is important, therefore, to radiograph the bones. Histological examination of bone-marrow obtained by trephining or puncture has also proved of value in diagnosis.

It has only recently been pointed out [11] that some cases of Gaucher's disease show thrombocytopenia and that in such cases the low platelet count is restored

to normal by splenectomy. The severe and constantly repeated hæmorrhages in Gaucher's original case [1] suggest that thrombocytopenia was present.

Splenectomy may be indicated as a palliative measure to relieve certain symptoms such as anæmia, purpura with hæmorrhages from the mucous membranes, or the pain and discomfort from the heavy viscus. It is not a curative procedure, nor does it prevent the development of bone involvement. In our patient a slightly low platelet count is present thirteen years after operation. The tendency to hæmorrhages has diminished. Its significance is now difficult to estimate, owing to the presence of hyperpiesia. But the operation has afforded the patient complete relief from abdominal pain and discomfort. It has also established the diagnosis.

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**Hyperparathyroidism. (Hyperfunction of a Parathyroid Tumour in a Case of Generalized Osteitis Fibrosa.)**—DONALD HUNTER, M.D.

M. M., married woman, aged 41.

*History.*—Nov., 1926: Pain in right knee on climbing stairs. No swelling of joint. Followed by pain in lower part of back and in left buttock, left hip and back of left thigh. Treated for sciatica for six months. March, 1927: Treated for prolapse of uterus by ring pessary. May, 1927: Was sent to a hospital for X-ray diagnosis. No radiograms were taken, but she was fitted with an abdominal belt. Went to an osteopath who told her there was "arthritis in the left leg." Had three or four "wrenchings" of left leg and cervical spine. Thoracic spine was "rubbed up and down, and it hurt a good bit." Aug., 1927: A specialist told her she had rheumatoid arthritis of left leg. Ten exposures to ultra-violet radiation "helped a little." Radiant heat treatment caused more pain. May, 1928: Unable to walk without sticks, pain in lower spine and right knee. Came to the London Hospital where Dr. R. A. Rowlands established a diagnosis of generalized osteitis fibrosa by radiograms of the bones. October, 1928: Attack of right lumbar pain with increased frequency of micturition and vomiting, subsiding after one week.

*Past History.*—No history of rickets as a child. Catamenia started at 14, still regular and normal. Married twenty-three years, four children alive and well, eldest 21 years, youngest 15 years. 1916: Fifth child born, died at age of four weeks; cause of death unknown. No miscarriages. In each case labour lasted about six hours, deliveries being normal. First baby weighed 8½ lb. 1922: Eight carious teeth in upper jaw extracted. 1924: All remaining teeth extracted for pyorrhœa.

*Family History.*—Father alive and well. Mother died at age of 32; cause of death unknown. Two sisters alive and well. No family history suggesting disease of bones.

*On Examination.*—February 1, 1929. (Patient admitted under the care of Dr. Robert Hutchison.) A thin poorly-built woman. Height 5ft. 1in. Weight 6st. 13lb. Calvarium normal in size and contour. Sclerotics white. Lenses normal on examination by slit lamp. Hearing normal. Double dentures. Tongue clean. Mucous membranes normal colour. No thyroid enlargement. No tumour felt in neck. Heart and lungs normal. Blood-pressure 140/90. No hypotonicity of muscles. No abnormality in nervous system. Trousseau and Chvostek signs absent. Kyphosis and diminution of lumbar curve. Tenderness on pressure over upper lumbar vertebræ and over sacrum which is unduly prominent. Pain in bones

of pelvis on striking iliac spines. No deformity of long bones, or bony swellings. No pain or limitation of movement on manipulation of hips or knees. Narrow subcostal angle, the lower costal margins approximating to the iliac crests. Thin pendulous abdominal wall. Right kidney enlarged, tender and mobile.

*Urine.*—Acid. Specific gravity 1010. Albumin $\frac{1}{40}$th. vol. Bence Jones proteose absent. No sugar. Deposit: Red cells and leucocytes. No tubercle bacilli found. The average daily output of urine (March-July, 1929) was 1,615 c.c. Urea concentration test: Second hour—1·14% (136 c.c. urine). Third hour—1·26% (112 c.c. urine). Phenol-sulphone-phthalein test normal. Blood-urea 0·048%.

*Radiograms of Bones* (see plates I to V).—Greatly diminished density of shadows of all bones examined. This is emphasized by contrast with the bones of a control subject of the same age, sex and build exposed simultaneously on the same negative. The sacrum, iliac bones, and right ulna are especially affected. Cyst-like areas, some of them trabeculated, are present in the right ulna, right tibia, right patella and in many phalanges of the right hand. There is erosion of the body of the third lumbar vertebra. The calvarium shows a uniform finely mottled appearance—Dr. S. G. Scott.

*Radiograms of Kidneys.*—Right kidney too low, but not enlarged. No calculi in kidneys or urinary tract. *Pyelogram.*—Right hydronephrosis.

February 26, 1929.—The patient had a further attack of right lumbar pain, and exploration of the right kidney was advised.

*Operation.*—Mr. Hugh Lett.—March 21, 1929. Right kidney explored. Pelvis enlarged. No obstruction found. No calculi. Nephropexy performed.

*Blood-count.*—Red cells 4,900,000 per c.mm., hæmoglobin 75%, colour index 0·65, leucocytes 8,080 per c.mm., differential count normal, bleeding time three minutes, coagulation time three minutes.

*Wassermann reaction* negative.

*Serum Calcium :—*

| | | |
|---|---|---|
| March 7, 1929 | 12·0 mgm. | per 100 c.c. |
| April 25, 1929 | 12·7 | ,, |
| April 27, 1929 | 13·5 | ,, |
| May 3, 1929 | 15·6 | ,, |
| May 10, 1929 | 13·2 | ,, |
| May 15, 1929 | 13·6 | ,, |
| May 29, 1929 | 16·5 | ,, |
| June 4, 1929 | 13·2 | ,, |
| July 12, 1929 | 16·7 | ,, |
| November 22, 1929 | 16·7 | ,, |
| November 25, 1929 | 15·8 | ,, |
| November 29, 1929 | 15·5 | ,, |

*Plasma Inorganic Phosphorus :—*

| | | |
|---|---|---|
| July 12, 1929 | 2·5 | ,, |
| November 22, 1929 | 1·0 | ,, |
| November 25, 1929 | 1·5 | ,, |
| November 29, 1929 | 1·7 | ,, |

*Plasma Phosphatase.*—Enzyme present in 1 c.c. of plasma liberated at least 1·9 mgm. P by hydrolysis from sodium $\beta$-glycerophosphate under standard conditions (normal 0·15 mgm.).—Dr. H. D. Kay.

*Calcium Output.*—The calcium output (see chart) was estimated in the urine and fæces over a period of fifteen days, during which the patient was kept on a weighed diet of low calcium content. The energy value of this diet was 1,975 calories daily. Sufficient alkali was given by mouth to make the reaction of the 24-hour mixed urine neutral to phenol-sulphone-phthalein (pH 7·3). During the fifteen days distilled water was used in the preparation of all her food and drinks. The fæces were divided into three-day periods by the oral administration of 0·3 grm. of carmine alum lake every third day. The urine was obtained in 24-hour specimens. The record of the calcium exchange is tabulated, the figures being milligrammes of Ca per three-day period.

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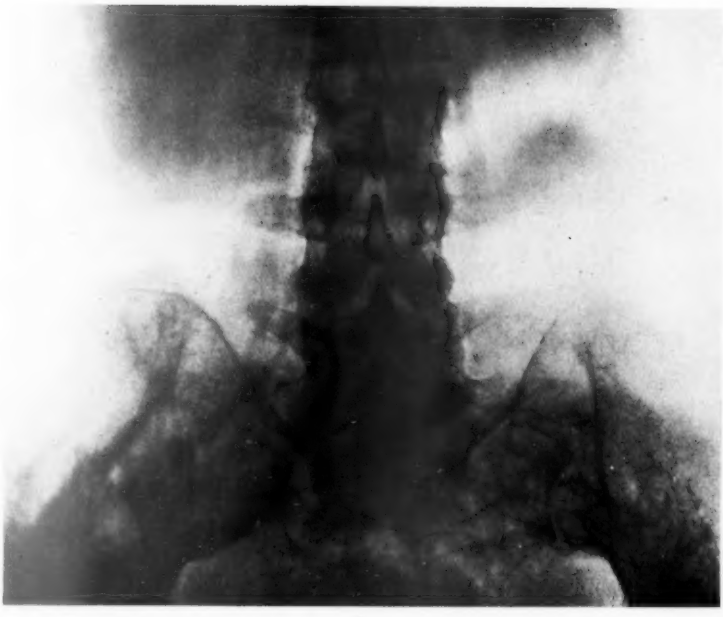
PLATE I.



*HUNTER: Hyperparathyroidism.* (*Hyperfunction of a Parathyroid Tumour in a Case of Generalized Osteitis Fibrosa.*)

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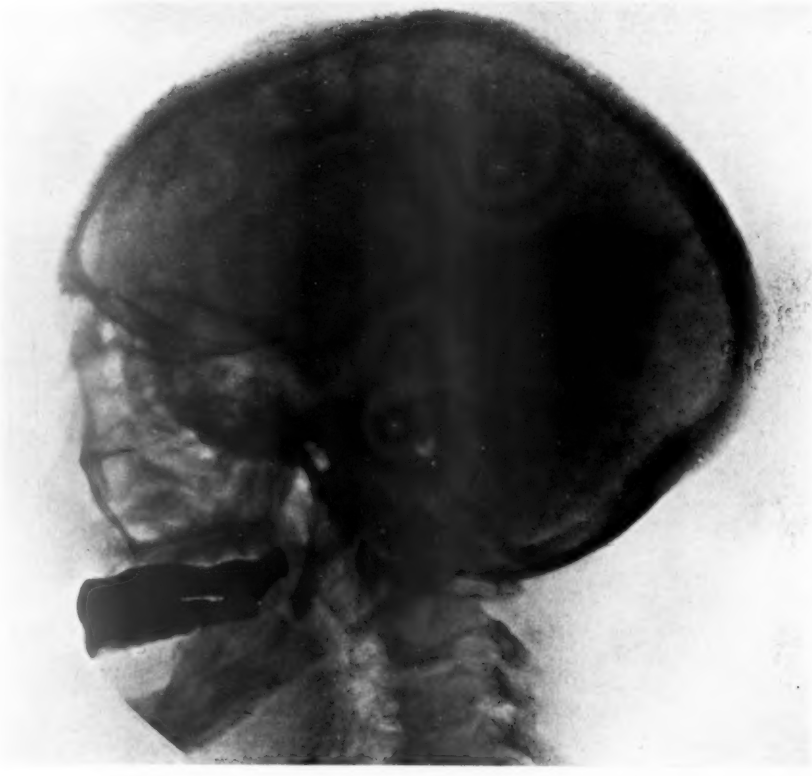
PLATE II.



*HUNTER: Hyperparathyroidism. (Hyperfunction of a Parathyroid Tumour in a Case of Generalized Osteitis Fibrosa.)*

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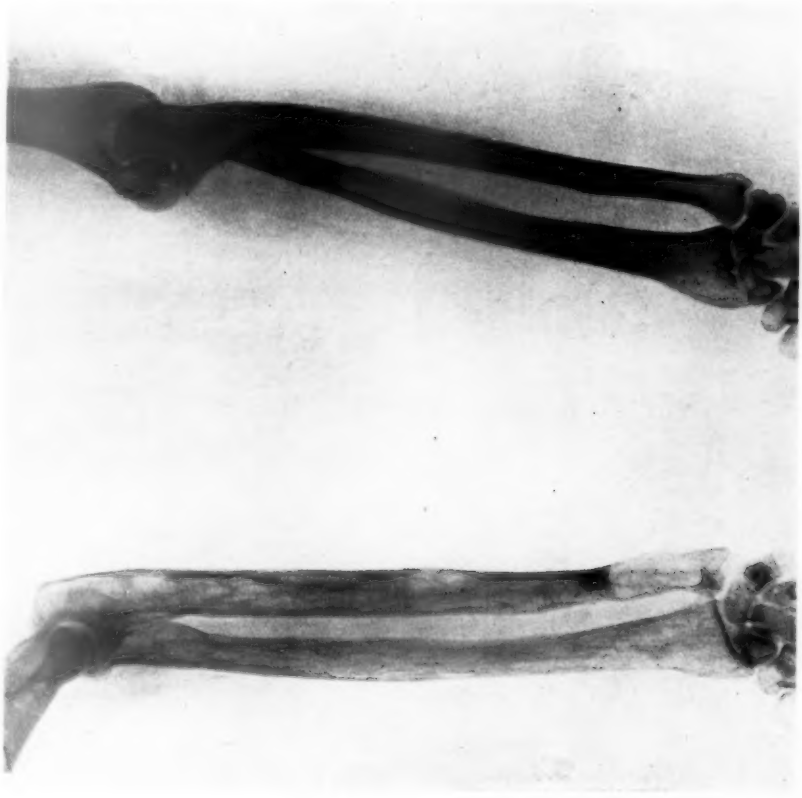
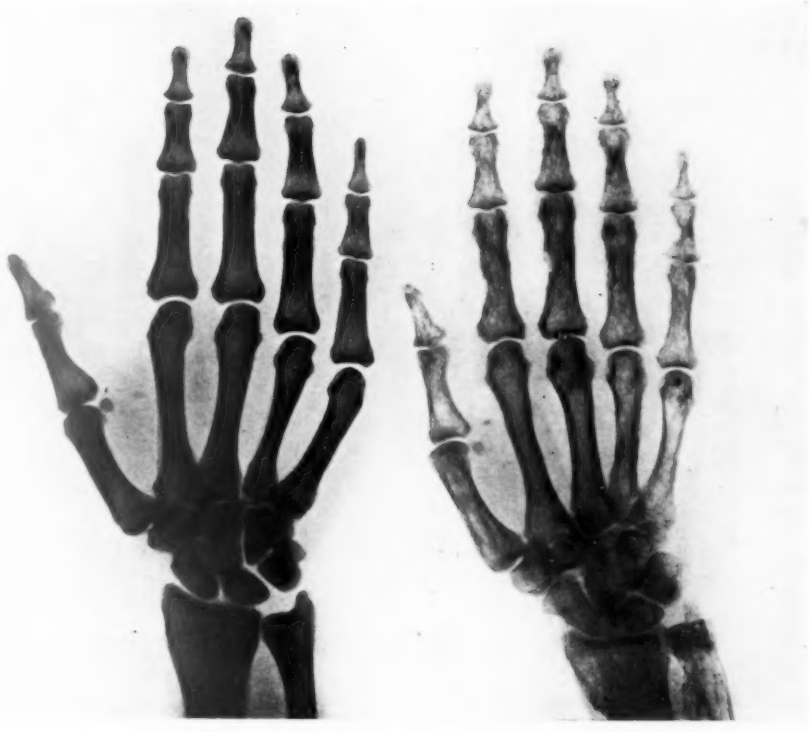
## PLATE III.

CONTROL



*HUNTER: Hyperparathyroidism. (Hyperfunction of a Parathyroid Tumour in a Case of Generalized Osteitis Fibrosa.)*

## PLATE IV.



CONTROL

*HUNTER: Hyperparathyroidism. (Hyperfunction of a Parathyroid Tumour in a Case of Generalized Osteitis Fibrosa.)*

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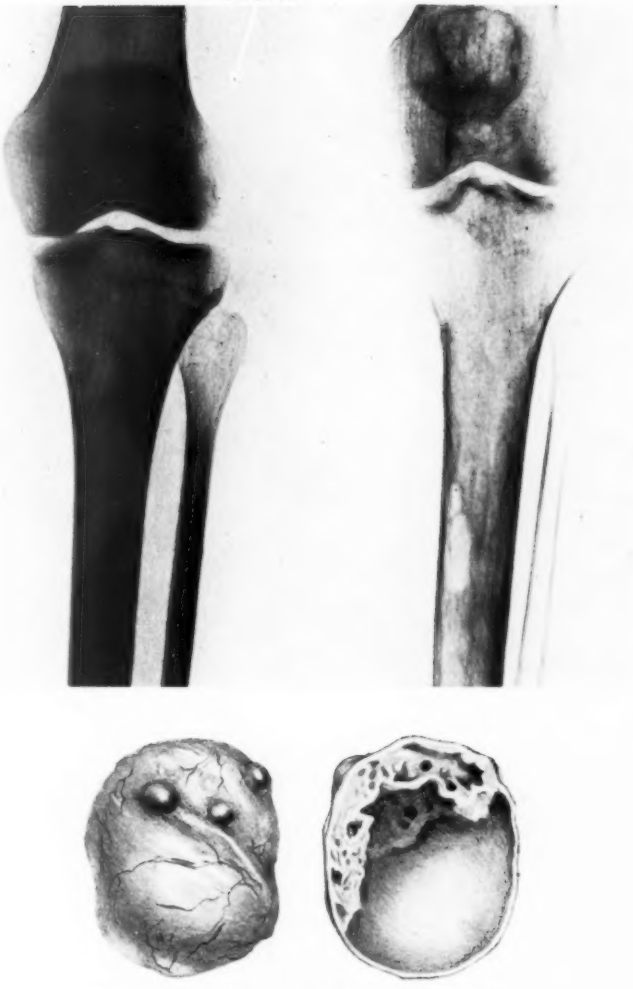
# PLATE V.

CONTROL



Tumour of left inferior parathyroid. (Actual size.

RECORD OF CALCIUM EXCHANGE.

| Three-day period | Calculated Intake | Output | | |
|---|---|---|---|---|
| | | Fæces | Urine | Total |
| I ... ... | 465 | 568 | 1299 | 1867 |
| II ... ... | 465 | 664 | 1550 | 2214 |
| III ... ... | 465 | 471 | 1481 | 1952 |
| IV ... ... | 420 | 700 | 1538 | 2238 |
| V ... ... | 413 | 525 | 1254 | 1779 |

*Progress.*—On completion of the above investigations the patient was discharged home on a diet of high calcium content (July 14, 1929). She walked with difficulty aided by sticks.

During September, 1929, she became worse. There was constant pain in the lower part of the spine and tenderness of the forearms and shins, on pressure. Shaking hands became painful owing to tenderness in the bones on compression of the knuckles. The arms and legs were weak so that she had difficulty in lifting things and in raising her feet to walk.

On November 10, 1929, she twisted her left ankle, causing a spontaneous fracture of the neck of the left femur. On November 20, 1929, she was readmitted. On examination there was great pain on attempting to manipulate the left hip. Pressure upon the shafts of the long bones, especially of the radius, ulna, and tibia, caused pain. On squeezing the hand there was pain in the heads of the metacarpals. In addition there was a smooth, firm, slightly tender swelling 4 by 1·5 cm. in the lower end of the right ulna corresponding to the trabeculated cyst-like area previously seen in radiograms.

*Radiograms.*—November 21, 1929: Considerable rarefaction of upper part of left femur especially the neck which is narrowed and shows a fracture without displacement.

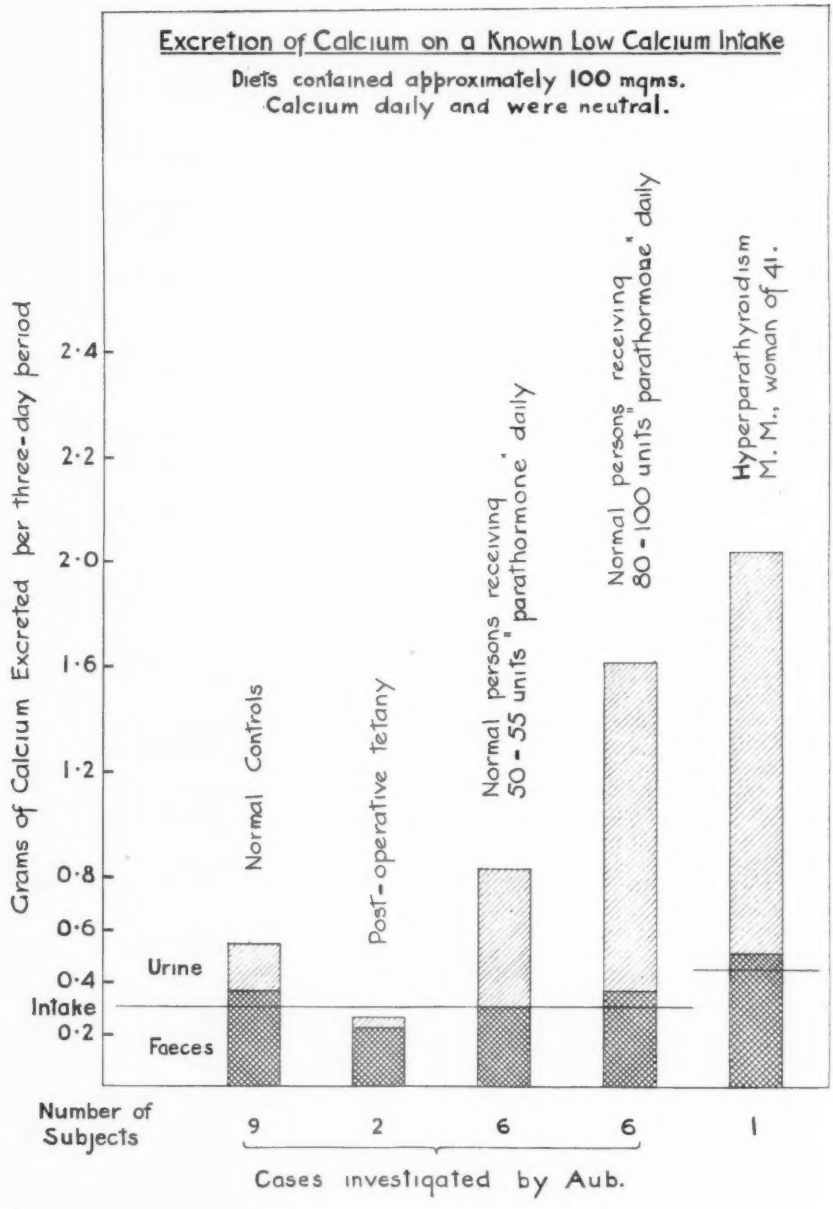
*Comment.*—Since the observation by Erdheim [1] in 1907 of enlarged parathyroids in osteomalacia more than a hundred cases have been reported of bone disease associated with hyperplasia or tumour formation in the parathyroid glands. The proof of hyperfunction in a parathyroid adenoma came also from the Vienna School when Mandl [2] in 1926 described the effects of extirpation of a parathyroid adenoma in a case of generalized osteitis fibrosa.

However, the real basis of our knowledge of the function of the parathyroids began in 1925 with the isolation by Collip [3] of their active principle. The rise in the serum-calcium brought about by parathormone (Eli Lilly preparation of parathyroid extract) was found to depend on an increased elimination of calcium from the bones [4], [5]. This effect is seen in the chart (p. 30). On a calcium intake of 100 mgm. a day, nine normal men are seen to be in negative calcium balance, whereas two patients with post-operative tetany are in positive balance. Administration of 50 units and of 100 units of parathormone in normal subjects is seen to cause a great increase in the output of calcium in the urine.

The last column in the chart represents the calcium output in the patient under discussion. Though the intake is higher than in the controls, it is evident that the excretion of calcium is equivalent to the continuous administration of about 120 units of parathormone per day. Knowing that the serum calcium is constantly raised to an average of 14·6 mgm. per 100 c.c. it is reasonable to suppose that the patient is suffering from spontaneous hyperparathyroidism.

The tenfold increase of plasma phosphatase is an interesting observation which cannot be adequately explained in the present state of our knowledge. The present patient is referred to by Kay [6] as Case 43 in his paper on this subject.

Much precise study is still necessary before the problems of normal ossification and of pathological deposition and resorption of bone begin to be understood. At present our methods of investigating mineral metabolism are crude, and this, no doubt, is the reason why we can pick out only so small a group of cases showing a


Excretion of Calcium on a Known Low Calcium Intake
Diets contained approximately 100 mgms. Calcium daily and were neutral.
Grams of Calcium Excreted per three-day period
2·4
2·2
2·0
1·6
1·2
0·8
0·6
0·4
0·2
Urine
Intake
Faeces
Normal Controls
Post-operative tetany
Normal persons receiving 50 - 55 units "parathormone" daily
Normal persons receiving 80 - 100 units "parathormone" daily
Hyperparathyroidism M. M., woman of 41.
Number of Subjects
9
2
6
6
1
Cases investigated by Aub.

definite disturbance of calcium and phosphorus metabolism. In the past three years we have estimated the serum calcium in a large number of cases of osteitis deformans (Paget), osteitis fibrosa (principally of the localized type), bone cysts and osteogenesis imperfecta. The present case is the only one in which hypercalcæmia was found. It should be noted that Kay [6] found increased plasma phosphatase in six cases of osteitis deformans (Paget).

*Treatment.*—A hyperfunctioning parathyroid tumour may be present without causing a palpable swelling in the neck. In the fourteen cases of hyperparathyroidism reported to date nine had no such swelling, but on exploration only two of these failed to show a parathyroid tumour. In these two cases it may be that a tumour was present and was not found. In most of the cases where a tumour was removed pain in the bones was abolished immediately after the operation and within some weeks or months the patient had considerably recovered from his disability. In the majority, too, the levels of the blood-calcium and phosphorus and the excretion of calcium in the urine were ultimately restored to normal. Temporary post-operative tetany often occurred, with wide variations in severity. It was fatal only in one case, namely, that of Beck [11], where two parathyroid tumours were removed. This is the only case of hyperparathyroidism recorded where more than one tumour was found. Some authors claim that an increase in density in the X-ray shadows of bones was to be seen in their cases a few months after operation. It is of great interest that three years after operation no such change could be demonstrated in Mandl's case.

It is because we have demonstrated parathyroid hyperfunction in this patient that we shall advise exploration of the neck in the hope of finding a parathyroid tumour. The disease is rapidly progressing and the prognosis without operation is clearly very poor. Should a tumour be discovered and extirpated it will be necessary to watch carefully for post-operative tetany and to have parathormone at hand as well as calcium chloride prepared for intravenous use.

The question of excision of a portion of the right ulna or great trochanter for histological section is important in establishing an accurate diagnosis of the bone lesions.

POSTSCRIPT.—*Operation* (Mr. A. J. Walton), November 29, 1929. Anæsthetist Dr. Ashley Daly.—Under intratracheal ether anæsthesia, a "collar" incision was made in the neck and the thyroid gland exposed by dividing the pre-tracheal muscles. The left lobe and isthmus of the thyroid were found to be normal. The left inferior parathyroid gland was replaced by a cystic adenoma measuring 3·7 by 3·0 by 3·0 cm. The tumour was deeply situated and was in immediate contact with the inferior pole of the left lobe of the thyroid. It was well encapsulated and was removed intact. The wound was closed without further exploration of the neck.

A portion of bone was removed from the swelling in the lower end of the right ulna.

*Progress up to the Tenth Day after Operation.*—Twenty-four hours after operation Chvostek sign appeared and has persisted every day since. On the second day pressure upon the bones caused much less pain than previously. On the fourth day, and subsequently, pressure upon bones caused no pain. There was a feeling of stiffness in the face and tingling in the fingers of both hands. On the ninth and tenth days this tingling in the fingers recurred. There has been no tetany, and Trousseau sign has been absent every day. The patient is much more cheerful than before the operation and is especially pleased to be relieved from the pains in the bones. The average daily output of urine since the operation is 850 c.c. (Urine: acid, specific gravity 1017, albumin-cloud; no sugar; deposit: leucocytes).

She has been on a diet of milk, ice-cream and eggs and there has been no need for calcium or parathormone therapy.

*Serum Calcium :—*

| | | | |
|---|---|---|---|
| November 30, 1929, | 11·6 | mgm. | per 100 c.c. |
| December 1, 1929, | 9·1 | ,, | ,, |
| December 3, 1929, | 9·9 | ,, | ,, |
| December 6, 1929, | 8·0 | ,, | ,, |

*Plasma Inorganic Phosphorus :—*

| | | | |
|---|---|---|---|
| December 1, 1929, | 2·8 | ,, | ,, |
| December 3, 1929, | 2·3 | ,, | ,, |
| December 6, 1929, | 2·0 | ,, | ,, |

Thus, forty-eight hours after the removal of the tumour the calcium and inorganic phosphorus values of the blood were restored almost to normal, and by the fourth day pressure upon the bones no longer caused pain. The post-operative findings, no less than the pre-operative, point strongly to the conclusion that the tumour was acting as a hyperfunctioning endocrine gland, and that this hyperfunction was primary in relation to the bone disease.

*Pathological Report by Professor H. M. Turnbull.*

*Naked-eye Appearance of Specimens removed at Operation.* (*S.D.* 2806. 1929.)

The specimen removed from the left side of the neck was a tense, fluctuating body measuring 3·7 cm. in length, and 3 cm. in breadth and thickness. (See plate V.) It was pyriform, the upper pole being slightly broader than the lower and the centre slightly constricted. Two silk ligatures were attached to a little areolar tissue on the upper pole. The central two-thirds of one surface were opaque and pale brown with a silvery sheen; in the remainder of this surface the opacity was interrupted by several raised, rounded, transparent areas, of which the largest measured 2 by 1 cm. These transparent, obviously cystic, swellings were blue purple. A leish of bright red vessels lay upon the upper pole and extended for a short distance upon this surface; on the opaque area were a few narrow, bright red and broader, purple vessels. The other surface was occupied by slightly raised translucent cysts of bright red to honey colour; in places a very thin silvery membrane lay over them.

On section a slightly opaque, blood-stained fluid escaped, and the specimen collapsed. The wall was seen to consist of a thin membrane, to the greater part of which was attached a lining of opaque, pale ochreous tissue, recalling suprarenal cortex. The ochreous tissue contained cavities from a pinhead to 0·4 cm. in diameter. A few of these cavities contained bright red blood; the remainder were empty. Its inner surface was broken into projecting trabeculæ, apparently by the rupture of cystic cavities. It was most abundant beneath the opaque area on the outer surface; here it measured 0·8 cm. thick. From much of the other surface it was entirely absent.

One half of the specimen was divided into four portions for fixation in: (1) 4% neutralized saline formaldehyde, (2) Zenker's fluid, (3) Bouin's fluid, and (4) absolute alcohol.

The specimen removed from the lower end of the right ulna was a slice of bone, measuring 1·5 cm. long, 0·5 cm. broad, and 1·3 cm. deep. Periosteum had evidently been removed from one of the narrow surfaces. This surface showed several longitudinal shallow linear depressions, and was otherwise smooth and silvery purple. One centimetre of the opposite surface was occupied by tough white fibrous tissue; the remainder was at a lower level, and resembled the sawn surfaces. The sawn surfaces were gritty and pink. An even, spongy structure of very fine mesh was suggested to the naked eye. A hand-lens showed closely-packed, projecting grey spicules in a pink ground. There was no trace of ivory bone.

The specimen was placed in 4% neutralized saline formaldehyde for subsequent partial decalcification in Müller's fluid.

(The histological findings will be reported later.)

It is a pleasure to thank Dr. Hutchison, Professor Ellis, Dr. Rowlands, Mr. Lett, Dr. Scott, Dr. Kay, and Professor Turnbull, for their co-operation in dealing with this case, Miss Simmonds, Miss Cass, Dr. Aitken and Dr. Ralston for carrying out

the laborious metabolism investigations, Mr. Walton for removing the tumour and excising a piece of bone, and Dr. Daly for giving the anæsthetic.

This work is part of a series of researches towards the expenses of which grants were made by the Yarrow Fund of the London Hospital Medical College (Dr. Hunter), the British Medical Association (Dr. Ralston), and the Ella Sachs Plotz Foundation (Miss Cass).

ABSTRACTS OF PUBLISHED CASES.

*Mandl* [2], *Vienna*, 1926.—Man, 38. Osteitis fibrosa of pelvis and both femora. Totally disabled by pain. Serum Ca 18·2 mgm. Increased urinary excretion of Ca. Parathyroid adenoma removed (25 by 15 by 12 mm.). Urinary Ca excretion dropped to one-eighth the pre-operative value. Three and a half years later no pain. Walks with a stick. Has gained 16 kilos. Serum Ca 13 to 14 mgm. No increase in density of X-ray shadows of bones.

*Lambie* [7], *Edinburgh*, 1927.—Woman, 30. Generalized osteitis fibrosa. Serum Ca 17 mgm., and inorganic P 2·7 mgm. On a milk diet Ca output in urine normal, but considerable increase in fæces. No operation. Diagnosis confirmed at post-mortem, and adenoma of parathyroid found.

*Gold* [8], *Vienna*, 1928.—Woman, 54. Osteitis fibrosa generalisata (von Recklinghausen) with cysts in right humerus and in three ribs. Mal-union of fracture of left femur. Serum Ca 13·1 mgm. Increased Ca excretion in urine. Parathyroid adenoma (25 by 15 mm.) removed. Serum Ca fell to 9·9 mgm. one month after operation. Five months later much less pain, serum Ca 9·6 mgm. Positive Ca balance. No increase in density of X-ray shadows of bones.

*Barrenscheen and Gold* [9], *Vienna*, 1928.—(Sex and age not stated.) Osteitis fibrosa cystica generalisata Recklinghausen. Pain in bones. Serum Ca 14·2 mgm. Slight increase of urinary Ca excretion. Removal of histologically normal parathyroid caused no clinical improvement. Two months later patient rather worse. Serum Ca 16·0 mgm.

*Duken* [10], *Jena*, 1928.—Case I.—Girl, 7. Osteodystrophia fibrosa. Pains in legs, tumour of frontal bone, protrusion of left eye. Tumour 2 cm. diam. in left side of neck thought to be enlarged parathyroid. Serum Ca 14 mgm., and inorganic P 5 mgm. No operation. (Post-mortem report unsatisfactory and incomplete.) Case II.—Girl, 14. Osteodystrophia fibrosa with late rickets. Ceased to grow at 12. Genu valgum. Hypotonicity of muscles. Polyuria. Fairly clear swelling in the neck (size and shape not stated). Serum Ca 20·8 mgm., and inorganic P 3 mgm. Resection of maxilla for tumour—histological examination showed osteitis fibrosa. No operation on neck.

*Beck* [11], *Kiel*, 1928.—Woman, aged 41. Generalized osteitis fibrosa. Amputation of leg for supposed sarcoma. Three years later fell and fractured femur. True nature of condition then recognized clinically, confirmed by X-rays and proved histologically. Six years after the fracture Ca and P levels in blood raised (no figures given). Urinary Ca excretion three times the normal. Two parathyroid tumours, size of almond and coffee bean removed. Three days after operation Ca and P values in blood normal, and Ca excretion in urine approximately normal. Tetany on fifth day, accompanied by a psychosis. Died of exhaustion on twentieth day.

*Du Bois and others* [12], *New York and Boston*, 1929.—Man, 30. Generalized osteitis fibrosa with extensive areas of decalcification and a large cyst in the right femur. Serum Ca 15·3 mgm., and inorganic P 2·1 mgm. Great increase in urinary Ca excretion. Exploratory operation on neck. No tumour found. Removal of two normal parathyroid bodies. Two years after operation little clinical improvement. Serum Ca 13·9 mgm., and inorganic P 2·6 mgm.

*Barr, Bulger and Dixon* [13], *St. Louis*, 1929.—Woman, 56. Osteitis fibrosa with benign giant-celled tumours of phalanx and ulna. Spontaneous fracture of clavicle. Hypotonia of muscles and joints. Increased frequency of micturition. Bilateral renal calculi. Serum Ca 16 mgm., and inorganic P 1·4 mgm. Great increase of urinary Ca excretion. Globular mass size of a small walnut felt embedded in left lobe of thyroid. Parathyroid adenoma removed (no measurements given). Severe tetany two days after operation. Calcium balance became positive. Swelling in superior maxilla became smaller.

*Wilder* [14], *Rochester, Minnesota*, 1929.—Woman, 35. Generalized osteitis fibrosa with giant-celled tumours of inferior maxilla and femur. Six years pain in hip ultimately affecting

all bones. Serum Ca 13·2 mgm., and inorganic P 1·9 mgm. Spherical mass palpable in neck: malignant adenoma of parathyroid removed (5 by 3·5 by 3 cm.). Three days later tingling in fingers and toes, but no tetany; serum Ca 7·1 mgm. Great improvement, gave up crutches. Four months later serum Ca 8·3 mgm., and inorganic P 1·8 mgm., increased density of X-ray shadows of bones.

*Boyd, Milgram and Stearns* [15], *Iowa City*, 1929.—Boy, 19. Generalized osteitis fibrosa. Progressive bowing of legs. Thirst and polyuria. Serum Ca 17·6 mgm., and inorganic P 2·2 mgm. Urinary Ca output three times the normal. Parathyroid adenoma removed (3·5 by 2·5 cm.). Chvostek sign appeared day after operation with serum Ca 12·3 mgm. Trembling of extremities with serum Ca 5·0 mgm., but no tetany. Polydipsia, polyuria and pains in limbs disappeared. After ten days calcium balance positive. Three months after operation blood Ca and P normal; bones showed evidence of progressive repair.

*Snapper* [16], *Amsterdam*, 1929.—Man, 56. Osteitis fibrosa generalisata (von Recklinghausen) with cysts in scapula and metatarsal. Totally disabled by severe pains in bones. Spontaneous fracture of femur. Under observation four years, during which time density of X-ray shadows of bones decreased. Serum Ca 23·6 mgm., and inorganic P 2·1 mgm. Greatly increased Ca and P excretion in urine. Tumour palpable in neck: parathyroid adenoma removed (25 by 15 mm.). Day after operation pains ceased. Tremor, acute mania. Chvostek sign with serum Ca 6·6 mgm. Ca excretion in urine fell to normal. Four months later great clinical improvement, serum Ca 10·6 mgm. and inorganic P 3·3 mgm. Fracture healed, and after five months X-ray shadows of bones were more dense. Able to walk after eight months.

*Eggers* (*quoted by Mandl*), 1929.—Woman (age not stated). Generalized osteitis fibrosa. Serum Ca 14·6 mgm. Parathyroid tumour size of hazel nut removed. Serum Ca reduced to 5·7 mgm. Definite clinical improvement. Death by accident. Post-mortem confirmed diagnosis.

*Lanz* (*quoted by Mandl*), 1929. (Sex and age not stated.) Generalized osteitis fibrosa. Parathyroid tumour removed. "Calcium values" immediately after operation had fallen quite characteristically.

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**Achalasia of the Cardia with Elongation and Extreme Dilatation of the Œsophagus.**—G. L. S. Konstam, M.D.—A. S., widow, aged 53, complained that for four years food seemed to lodge at the lower end of her breast-bone. Solids and liquids often regurgitated unchanged a few moments after being taken and her appetite had disappeared. She had lost several stones in weight.

*Condition on Examination.*—Very emaciated woman. Right pupil smaller than left but both react normally to light and accommodation. Otherwise no abnormal physical signs.

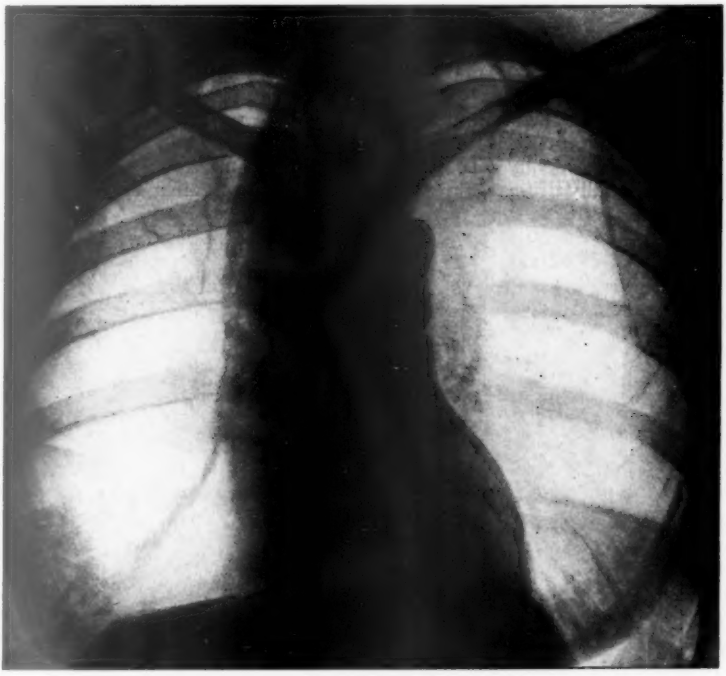
A provisional diagnosis of achalasia of the cardia was made and an X-ray examination requested. The particular interest of this case lies in the confusing radiographic appearances.

The first skiagram showed an elliptical shadow extending down the whole length of the thorax immediately to the right of the vertebral column. But for the fact that the lung markings extended to the thoracic wall the appearances suggested pneumothorax with collapsed lung. A small amount of barium was swallowed by the patient and delay at the level of the aortic arch was reported (Dr. M. Schwartzman).

It was not until a barium meal examination of the stomach was requested that the true state of affairs was realized.

In the second skiagram the barium was seen to have filled an enormously dilated œsophagus. Elongation has caused the œsophagus to deviate to the right and to undergo an S-shaped bend at its lower end.

The third skiagram was taken after the œsophagus had been washed out with several gallons of fluid, with the result that the paravertebral shadow seen in the first skiagram is now very faint. The œsophageal shadow is therefore due largely to accumulated food débris and not to thickening of its wall.



Achalasia of the cardia. (Dr. Konstam's first case.) Skiagram (without barium) showing paravertebral shadow produced by food débris in dilated œsophagus.

The confusing result of the first barium meal examination is accounted for by the use of insufficient barium which trickled slowly through the large œsophageal food residue. Van der Mandele,[1] in 1926, showed how the X-ray shadow of such an œsophagus could be confused with that of the right border of the heart.

Several attempts at passing mercury bougies into the stomach, with and without œsophagoscopy, failed owing to the double kink above the cardia.

The patient now lives on a semi-solid diet and has learned to wash out her œsophagus twice a day. She has gained nearly three stones in weight.

Dr. F. PARKES WEBER said that he had gradually come to the conclusion that in at least some of these cases the primary condition was an "idiopathic" congenital-developmental enlargement of the œsophagus ("megalœsophagus") analogous to the "megalocolon" of Hirschsprung's disease, the involvement of Auerbach's and Meissner's nerve-plexuses,

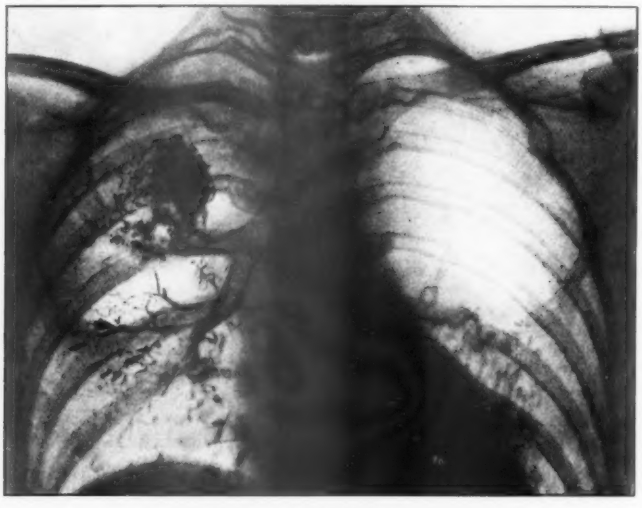
1 Van der Mandele, *L. J. Fortschr. der Roentgenstr.*, 1926. 34.84.

with achalasia or spasm or mechanical obstruction at the cardia, being secondary. This explained how "megalœsophagus" might sometimes be symptomless and discovered by X-ray examination of the thorax undertaken for some other purpose.

**Interlobar Empyema with Rupture into a Bronchus.**—G. L. S. KONSTAM, M.D.—D. B., female, aged 24. *History.*—December, 1928, appendicectomy (normal appendix). Three days later a cough developed with copious sputum. After many weeks in hospital patient returned home and in June, 1929, she suddenly coughed up two pints of offensive sputum. *Past History.*—Pneumonia five years ago.

*Condition on Examination.*—Wasted, pale woman. No cyanosis, no clubbing. Heart not displaced, no murmurs.

*Respiratory System.*—Sputum copious, purulent, and offensive. Trachea central. The right chest is flattened and shows diminished movement. Over right zone II posteriorly, percussion note is impaired and cavernous breath sounds, bubbling râles and whispering pectoriloquy may be heard. Crepitations are present at the bases. The sputum gradually decreased from 16 oz. to 1 oz. per diem, and on microscopic



(Dr. Konstam's case of interlobar empyema.)
Skiagram showing lipiodol filling abscess cavity in right upper lung field.

examination, sarcinæ and coliform organisms were found. The sputum was examined for tubercle bacilli on six occasions, with negative results.

The temperature which was at first remittent tended to settle at the end of the patient's nine weeks' stay in hospital, and she gained 7 lb. in weight. No special treatment was employed.

*X-ray Examination after Intratracheal Lipiodol Injection* (Dr. G. Vilvandré).—Communicating with the right upper bronchus is seen a large oval cavity filled with lipiodol. The speckled appearance at the periphery is doubtless due to the incomplete admixture of the opaque material with pus present in the cavity. We have been exceptionally fortunate in filling the abscess cavity; usually pus or inflammatory thickening of the bronchial mucosa blocks the bronchus into which the abscess has burst.

I have to thank Dr. Cecil Wall for permission to show this case.

JOINT DISCUSSION NO. 1.

# Section of Obstetrics and Gynæcology, and Section of Comparative Medicine.

[*October* 18, 1929.]

## DISCUSSION ON THE CAUSES OF EARLY ABORTION AND STERILITY.

**Professor Arthur Robinson:** When the term sterility is used in association with human beings, it is commonly applied either to the male or the female of a pair, the inference being either that the one or the other is incapable of producing normal mature germ cells or that the male is unable to transmit, or the female to receive, such cells. From a biological point of view, a wider—yet at the same time a more precise—definition seems desirable, when bisexual animals are being dealt with, since though neither the male nor the female of a pair may be sterile, the pair may be so. Fertility is obviously necessary for the continuance of the species, therefore sterility might be defined as the incapability of a pair of bisexual animals to produce young which live to the reproductive period and are themselves fertile or, in a narrower sense, the incapability of a pair of bisexual animals to produce living young.

If the definition is accepted, then we may say that there are two types of sterility: (1) intentional and (2) unintentional.

Intentional sterility is confined to human beings, and although it is sometimes associated with abortion it is primarily a sociological question and needs no further consideration to-night.

Unintentional sterility is common to all bisexual animals, and may be due to one or other of several causes:—

(1) Injury of the genital organs of one or both of a pair; (2) Malformation of the genital organs of one or both of the pair; (3) Disease of the genital organs of one or both of a pair; (4) Incapability of one or other or both of the pair to produce mature germ cells; (5) Incapability of one or other or both of the pair to produce normal gametes; (6) Incompatibility of the gametes produced by the pair.

(1) and (2) Injuries and malformations are of surgical interest, but they are, perhaps, of secondary concern in to-night's discussion, although in certain cases they may be associated with abortion.

(3) Sterility and abortion caused by disease of the genital organs I leave to my clinical colleague to discuss, as they fall naturally into his domain.

(4) The incapability of the sex glands to produce mature gametes could be diagnosed in the case of the male by the examination of the semen, but I do not know how it could be diagnosed in the female, except by the elimination of every other possible cause, for in the case of the human female, menstruation is no criterion of ovulation, and in other mammals the pro-œstral and œstral phenomena, though usually associated with the maturation of ovarian follicles, can occur independently, according to the observations of A. S. Parkes.

The researches of E. T. Smith and E. T. Engle have shown that the maturation of the gametes is under the control of the anterior lobe of the pituitary body, but although absence of mature gametes would inevitably result in sterility, it could not possibly be associated with abortion, and therefore it needs no further consideration here.

(5) The fifth group of causes of sterility, the incapability of one or other, or both of the pair, to produce normal gametes, may be looked upon by some as purely speculative. Admittedly, it would be difficult to prove that an extruded mature ovum was not normal at the time of extrusion, but Savage and Williams and Fowler have shown the heads of the spermatozoa of bulls differ in size, and that, in the case of any given bull, if the heads of the spermatozoa vary in size beyond certain narrow limits, the bull is not a good sire; either it is impotent, or its service is followed by abortion, or its progeny are unsatisfactory. This being the case, it is not unfair to assume that the arrangement of the chromatin particles in the ovum, or the spermatozoon, or both, may be such that it will not prevent fertilization, but will prevent the formation of a normal zygote, from which a normal embryo can be evolved. If such a state of affairs occurred in one or other, of both of a human pair, it might be associated with sterility, which very possibly would be associated with repeated abortions, exactly as I hope to show that sterility may occur and be associated with abortion in my sixth group of cases, in which sterility is due to the incompatibility of the gametes produced by a pair of animals.

It has been a general belief that every extruded ovum will, under favourable circumstances, unite with a spermatozoon to form a zygote, from which a normal new individual will be evolved; but when inquiry is made into the number of ova shed by any given group of animals, placed in the most favourable circumstances for fertilization, and the number of young produced, a great discrepancy is disclosed. In many animals not more than two-thirds of the shed ova are followed by living young, and in some cases more than half the shed ova fail to be converted into new individuals. During a period of five years, of 3,640 ova shed by thoroughbred mares, 58·68% failed to produce foals, although the mares were mated with stallions under the control of the Scottish Board of Agriculture, and during a period of six years, of 28,248 ova shed by Clydesdale mares, 48% failed to produce foals after the mares had been mated with healthy Clydesdale stallions.

What became of the ova which did not produce foals is not known; some may not have been fertilized, some may have united with spermatozoa to form zygotes which died soon after their formation and were cast off. Abortion at an early stage in the case of mares, is very likely to escape notice, and of those ova which produced foals which died before birth there is no record, therefore it is necessary to seek elsewhere for information as to what becomes of the shed ova placed in favourable circumstances for fertilization which do not produce living young. The obvious source is some group of animals not too expensive and not too large which can be inseminated easily under observation, and which can be killed at various periods after insemination, so that the number of ova shed can be found from the number of corpora lutea in the ovaries, and the number of zygotes in the uterus can be counted. The animals I chose for the purpose were ferrets. The number of animals used, and suitable for the investigation, was 165, the number of the ova shed was 1,643 and of those over 30% failed to produce living young. By making serial sections of the oviducts and the uteri, in the early stages, and sections of zygotes and embryos which were evidently not normal, in later stages, it became possible to determine what had happened to the majority of the shed ova which failed. The examination showed that some of the shed ova had not been fertilized, although plenty of spermatozoa were present. The presumption in their case was that they were unable to unite with the available spermatozoa. The majority of the ova had united with spermatozoa to form zygotes, but about 39% of those zygotes failed to give rise to living young.

A review of the whole series made it clear that death might occur at any time between the initiation of the zygote and fertilization, and the forty-second day thereafter, when the fœtus would have been born had the zygote been normal.

If death occurred in the earlier stages, either before or after the attachment to the uterine wall, absorption of the degenerated zygote took place, and, thereafter, the uterine mucosa, in the situation of the gestation chamber, returned to a normal condition. If death occurred in the later periods, the dead fœtus was extruded from the uterus with the living young at the normal birth period.

In the case of animals which produce multiple young at birth, the death of one of the zygotes is not followed by its abortion, for such an event would necessitate the destruction of the rest of the brood, but in the case of animals which normally produce only one youngling at birth, if the death of the zygote occurs after the attachment to the uterine mucosa has taken place then abortion follows, for that is the quickest way of enabling the uterine mucosa to be prepared for the reception of another zygote.

In the case of the ferrets and other multiple-bearing animals, the dead and degenerating zygotes are situated most commonly between normal zygotes which are —and have been—subject to exactly the same conditions, therefore their deaths could not be attributed to disease of the mother, to hormones or vitamins, and there was no indication that they had suffered any mechanical injury. The only possible conclusion seems to be that the chromatic constitution, established at the time of fertilization, was not adequate to produce a zygote capable of developing beyond a certain period, shorter or longer as the case might be.

It can scarcely be doubted that the incompatibility of gametes, which occurs in all mammals which have been examined, occurs also in man, and as it appears to be the more prevalent the more highly specialized the animal is, it is probably very prevalent in man, accounting for cases of sterility without abortions, and for sterility with repeated abortions, for both of which there is no treatment except divorce and remarriage.

Further, it cannot be doubted that this incompatibility is the cause of many abortions not associated with sterility; in such cases the condition of the uterine mucosa found after the abortion is not an indication of disease, it is merely the condition of a mucosa doing its best to return to a state adapted for the reception of another zygote.

**Mr. J. R. Barker**: To throw sterility into close juxtaposition with early abortion is justifiable; one condition gradually merges into the other. Early abortion in cattle might conveniently be studied from the starting point of a fairly easily observed abort, say that of thirty-one days. Such an abort with its unruptured membranes has a capacity of at least twenty ounces and can be termed macroscopical; it is, moreover, exceedingly rare. An abort, with fœtal envelopes, of shorter intra-uterine duration, is smaller, until one reaches the stage at which an abort may simply be a microscopical morula. Indeed such a condition might very well be termed the immediate post-sterility stage.

The causes of early abortion in cattle may be said to commence with the lack of power of the fertilized ovum, or morula, to absorb nutrient materials necessary for its further development. A faulty spermatozoon uniting with a functioning ovum might produce such a morula. Much time and thought has been spent upon defining the diseases which might lead to the formation of imperfectly functioning spermatozoa. Orchitis due to streptococcic infection is the most important in cattle. Microscopical examination of the semen of clinically affected bulls, or bulls from herds with a high abortion or sterility rate, reveals such faulty spermatozoa. Such samples of semen may exhibit a sluggish motility which soon disappears. Uniformity of heads is accepted as a fairly accurate estimation of function. Conversely, where this uniformity is lacking, is a sign of impaired function. It can readily be understood that should such a spermatozoon fertilize a faulty ovum, and the two are frequently produced in a diseased herd, the resultant morula will perish.

In the absence of suitable nutrient materials a healthy one might perish, but an imperfectly functioning one is sure to do. In cattle the uterine glands secrete uterine milk which makes available sources of nutriment for the recently descended morula. A previous infection with the *Bacillus abortus* acting as a Gram-negative organism, on the capillaries and small blood-vessels of the uterus, leads to the entire absence of this uterine milk. In the course of a research carried out in conjunction with the late Professor E. Glynn, sterile cows which had been the subject of infection with the *Bacillus abortus*, and whose breeding records were known, were slaughtered. Sections of the wall of the uterus indicated endarteritis obliterans, and a lack of staining power on the part of the epithelial cells of the mucous membrane. I presume that such a uterus could not provide suitable nutriment for a recently fertilized ovum. In fact it might even lead to the presence of deleterious materials being present in the uterus. Should this blocking of the arteries of the womb proceed to a further stage, necrosis with sloughing of the maternal cotyledons takes place. Such a cow with absence of cotyledons or true placental areas is frequently brought to the notice of the veterinary surgeon who happens to be a "remover" of retained membranes. A definitely diseased mucous membrane following infection with the *Bacillus abortus*, would appear, from Professor Glynn's specimens, to be fairly frequent. Tuberculosis is not nearly so common. In any of the foregoing, the end result is the same: the fertilized ovum, morula, or fœtus perishes and is expelled. Abortion, either unobserved or observed, is the result.

Sterility in cattle is only a previous state to an early abortion, and indeed the two may be clinically indistinguishable. It follows that sterility is due in the main to the same underlying disease-causing agencies. Any investigation of the cause of sterility in a female is incomplete without an examination of the male; orchitis, epididymitis, inflamed and enlarged vesiculæ seminales are encountered as a result of such an examination. Microscopical examination of the semen reveals faulty and diseased spermatozoa, and also pathogenic organisms. I have observed streptococci, staphylococci and Gram-negative bacilli in stained smears from bulls with bad breeding records. Such a bull, mated with a susceptible female, would infect and set up disease processes in that female. Sterility after that copulation would be one result, but infection of the female, leading to vaginitis and ovaritis, would be another result. Subsequently, without treatment, such a female is offered in service to another bull, possibly producing more perfectly functioning spermatozoa. This leads to another cause of sterility, failure of the functioning spermatozoon to reach the ovum. This may be due to a vaginitis. Streptococci, Gram-negative bacilli and Gram-negative cocci are to be found in vaginal smears from sterile cows. Cervicitis is a frequent cause of the failure of the functioning spermatozoon to reach the desired haven. The cervix of the female bovine is peculiarly tortuous, liable to injury and subsequent infection, or to an extension of a vaginitis contracted at coitus. Such a cervix acts as a barrier to the passage of active male elements. Endometritis, produced in the manner aforementioned by the *Bacillus abortus*, or other organisms acting on the capillaries of the uterine wall, can prevent the passage of the sperms. Salpingitis, due to an extension of a metritis of a previous pregnancy, is sometimes encountered. The failure of the ovary to produce a functioning ovum is a very frequent cause of sterility in cattle. Contrary to the experiences of most writers on sterility in cattle, I frequently encounter swollen and enlarged ovaries. In a great proportion of these cases of enlarged ovaries there is a concurrent vaginitis. It would appear that the disease process skips the body of the uterus and the uterine cornua. After a recent infection there is an absence of œstrum for a period of from six to nine weeks, and thereafter œstrum is manifest at varying intervals of ten, fourteen and eighteen days. There does not appear to be any known method of accurately estimating whether an ovary is producing a perfectly functioning ovum. In the female known to have been the subject of disease an œstral period of

nineteen, twenty or twenty-one days is the only guide. Finally a salpingitis may prevent a functioning ovum from reaching a position in the Fallopian tube favourable for fertilization.

In discussing the causes of abortion and sterility, one has to remember that cattle are bred and reared on the herd plan. Frequent additions are made to the herd, both of males and females. These additions bring the genital diseases of the herd from which they came; they sometimes cause a spread of these infections amongst the older members of the herd, or the herd suffers a lighting up of a previous latent infection due to the introduction of fresh migrants. Polygamy is the rule. Males and females are infected at coitus. Communal bulls spread infection far and wide over the various herds of the district in which they are situated. Subsequent sterility cases are mated with all the bulls in the district before they are abandoned as breeders.

**Professor Beckwith Whitehouse:** In attempting to solve the varied problems associated with the causes of early abortion and sterility, my colleagues have shown wisdom in inviting the co-operation of the Section of Comparative Medicine. Premature expulsion of the living or dead ovum from the uterus is not a phenomenon confined to the genus Homo, and a knowledge of the factors which influence its occurrence in other organisms is of more than usual interest to those of us responsible for its prevention and treatment in the human species.

The phenomena of ovulation, fertilization and development of the ovum involve problems of great complexity in which the aid of the anatomist, the physiologist and the biochemist must be sought before we can hope to understand the factors which lead to the early death and premature expulsion of the products of gestation from the uterus.

Abortion in the human species is a common occurrence, more common in some countries and communities than others, probably owing to the artificial termination of pregnancy. It has been stated on reliable authority that the number of abortions each year in Germany is between 500,000 and 875,750, and that in Hamburg in 1919 one abortion occurred for every two births. In this country, I am glad to say, the figures do not attain any such dimensions. Investigations, based on 3,000 patients admitted to a gynæcological clinic, and covering pre- and post-war years, show an incidence of one abortion to every 4·7 births. In 11,430 pregnancies the percentage of abortion was 17·2; and in 3,009 women the percentage who had aborted at some time or other during their sexual life was 35·3. These details are shown in Table I.

The criminal practice of the termination of pregnancy vitiates, of course, the value of figures as a guide to the frequency of natural abortion. We are not now concerned with the artificial termination of pregnancy, by mechanical means or by drugs, but only with the causes which underlie the natural expulsion of the developing ovum.

For a gestation to progress in a normal manner to Nature's appointed goal, certain fundamental axioms must be established: (1) The germ plasm of the oöcyte and the spermatozoon must possess adequate initial vitality. (2) The zygote must be implanted in a favourable position for its subsequent development. (3) The nutrition of the ovum must be maintained by an adequate supply of food elements in a suitable environment.

Each of these factors provides a fertile field for discussion.

*Initial Vitality of the Germ-plasm.*—In the first place, can any facts be adduced to show that defective vitality of the germ-cells leads to impaired development or premature death of the fertilized ovum? Direct evidence is difficult to obtain, but some information may be gained by a study of the incidence of abortion in relation to parity. Table II is an analysis of 1,233 cases showing the number of abortions in relation to parity. In the case of 336 childless women, 265 were sterile on a five-year basis. The remaining 71 aborted at each pregnancy

in the proportions shown in the table. It will be noted that whilst 47 had one abortion, 3 had four, and 2 as many as five consecutive disasters. It may, of course, be argued that environment, e.g., a diseased uterus, was the cause, and not defective vitality, but it is difficult to believe that such environment is the common factor in the case of all these sterile women.

As parity increases, there is a progressive increase in the incidence of the number of women who abort, as shown in Table III. Although failure of reproductive power may be the deciding influence, other factors are necessarily introduced, and therefore I do not use these figures to substantiate the argument. From time to time, however, cases occur which throw more light on the problem. I will quote one such instance :—

Mrs. L., aged 33, married for five years, was delivered of a dead child at the seventh month of her first gestation without any obvious cause. She is a small undersized individual, weighing 7 st., and is herself a seven-and-a-half-months child, and the last of a family of thirteen. Her mother, also a premature child, was the last of a family of sixteen. Mrs. L's immediate brothers and sisters were all premature. Two were stillborn, one has tuberculosis, and the other a congenital cardiac lesion.

This remarkable genealogical tree of a macerated fœtus points, I think, to inherent defective vitality of the germ-plasm, the result of exhausted reproductive capacity.

The offspring of senile parents is, in my experience, often abnormal in some ways, although I cannot bring forward any evidence of the undue frequency of abortions in such individuals.

*Implantation of the zygote.*—The site of implantation of the fertilized ovum is an all-important factor in its subsequent normal development. Abnormal implantation almost always leads to disaster. The natural and normal site of attachment of the zygote is the decidua of the upper uterine segment. In the lower uterine segment the decidual organ is much less developed, and implantation in this area is, I believe, commonly followed by death of the ovum. From my own experience I am convinced that when abortion occurs after the twelfth week of gestation it is often associated with a low placentation in the region of the os internum. The development and function of the decidua call for special consideration in its relation to abortion. It is now generally accepted that the growth of the endometrium is stimulated and maintained by a hormone elaborated in the corpus luteum of the ovary. If this hormone is withdrawn by destruction, excision, or even aspiration of the corpus luteum, necrosis of the decidua ensues, followed by abortion of the developing ovum. This fact, originally demonstrated by Fränkel, has since been confirmed by many observers.

Recently Teel and Parkes have shown that lutein development is controlled by the anterior lobe of the pituitary gland, and that sensitization of the endometrium and development of artificial placentomata can be stimulated in the rat during the di-œstrus cycle by the administration of sodium hydroxide extracts of the anterior lobe. The normal development of the decidua is a complex phenomenon and dependent upon more than one factor. Not only the endometrium, but also the ovary and pituitary gland assume, therefore, considerable importance in relation to abortion. In the case of uterine fibroids and also in retroversion of the uterus, associated with prolapse of the ovaries, the Graafian follicles and corpora lutea frequently demonstrate pathological lesions, owing, I think, to circulatory changes, especially interference with the venous and lymphatic return. Both these conditions are commonly associated with sterility and abortion, and the cause in each may be defective function of the corpus luteum.

A cystic condition of the corpus luteum has long been known to be associated with abnormal pregnancy, e.g., tubal gestation, and vesicular mole. A similar cystic state of the lutein body existed in the case of two carneous moles in which I had the opportunity of investigating the ovaries.

Possibly inhibition of the corpus luteum and consequent necrosis of the decidua may be the cause of abortions attributed from time to time to mental or physical shock. The abortion rarely ensues immediately upon the stimulus, but commonly

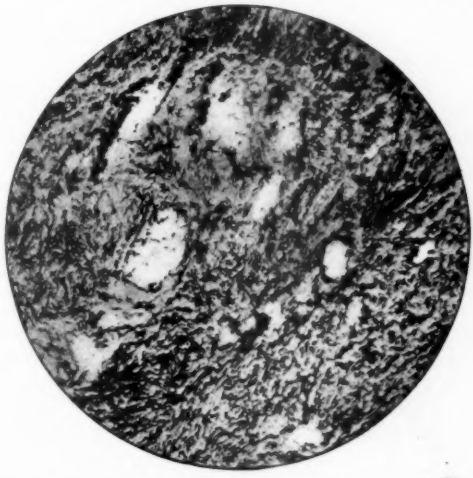


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FIG. 1.—Ovarian stroma (human) stained by Bielschowsky's method. Showing nerve fibrils.

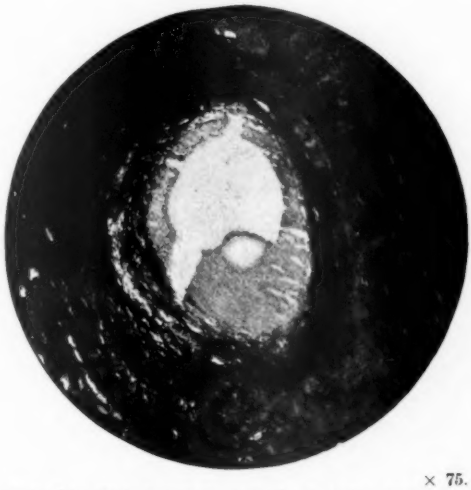

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FIG. 2.—Human ovary stained by Bielschowsky's method. Showing great concentration of nerve fibres round Graafian follicle.

occurs a few days later when, presumably, necrosis of the decidua has taken place. We know little about the innervation of the ovaries, but sections stained appropriately show a complex system of nerve fibres and ganglia in relation to the Graafian follicles and capillary vessels in their immediate proximity (figs. 1, 2 and 3).

Turning to the endometrium itself, it is obvious that its integrity and power to respond to sensitization by the lutein hormone are essential factors for the normal implantation of the zygote. If it is abnormal in development as in the case of a uterus, the seat of fibromyomata, or chronic subinvolution, or injured by repeated attacks of chronic inflammation, it is more than probable that it responds to the lutein stimulus in a defective manner, with the result that the zygote develops in an abnormal environment.

The pathological conditions associated with 300 women who gave a clinical history of three or more abortions are shown in Table IV. It will be noted that uterine lesions were present in 53·3 per cent. Evidence of chronic inflammation in the pelvis, either in relation with the genital tract or pelvic peritoneum, was present in 26·6 per cent. of the cases investigated. The importance of an abnormal environment to the developing ovum is stressed by embryologists and is a point to which obstetricians have given perhaps too little attention. It is a remarkable fact

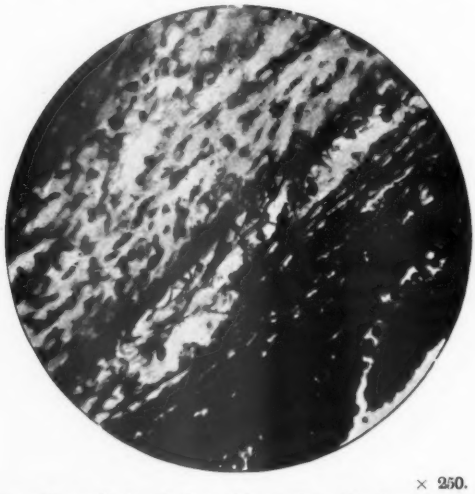

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FIG. 3.—Nerve fibres and ganglia in relation with capillary blood-vessel in immediate proximity to the "granulosa" cells of the Graafian follicle.

that a large proportion of ova which are aborted are abnormal. The largest number of abortions occurs during the second or third months of gestation. Mall states that 50 per cent. of ova which he examined during the first two months of gestation were pathological. Mall's figures are in excess of those given by His, but cover a larger amount of material. The figures of His and Mall are given in Table V, whilst Table VI shows in detail the variations noted in Mall's series.

It is unnecessary in the present discussion to consider in detail the various types of abnormal embryo described by different observers. Sufficient be it to note that in one group the embryonic mass is composed only of a nodule representing the umbilical vesicle. In a second group the chorion only exists, there being neither amnion nor umbilical vesicle. In yet another group the embryo is destroyed after development of the amnion, and is represented by a granular mass or perhaps only by the stump of the umbilical cord.

Many, perhaps the majority of early abortions that fall into our hands, are useless for investigation, owing to damage and rupture of the amniotic sac. Since,

however, I have been interested in the question of abortion and have been on the look-out for material, quite a number of complete abnormal ova have fallen into my hands, confirming the views expressed to me by the late Professor Peter Thompson, and those of other embryologists. One of the specimens I have obtained and which I bring before the Section this evening, consists of the chorion and amnion only. There is no trace of the embryo, according to the report of Professor Brash, of the Anatomical Department of the University of Birmingham, to whom the ovum was referred. The gestation sac was spontaneously expelled intact from the uterus of a patient—Mrs. W., aged 30—during the course of her third pregnancy. The previous pregnancy had also terminated by abortion at the fifth week. The first gestation had progressed to term naturally, and ended with the birth of a healthy girl. The patient had been treated for backward displacement of the uterus, and both abortions were attributed, rightly or wrongly, to the uterine malposition.

I have already referred to the possibility of defective decidual development in cases of uterine displacement resulting from abnormal lutein function in prolapsed ovaries. Further information is required on this point, and the ova expelled from retroverted uteri should be carefully investigated for evidence of abnormality, together with the decidua curetted from such uteri. Lesions are not confined to the embryo in many of these aborted ova. Disease of the chorion is equally common, and the two usually coincide. Various pathological changes are seen. The most constant and earliest evidence of a pathological state is the presence between the chorionic villi of a mucoid substance containing numerous leucocytes. The syncytium grows into this mass, not in a normal radiating manner, but in irregular masses and clumps. In some cases syncytium and leucocytes actually invade the mesoderm of the chorion. In other instances the chorionic villi are few and far between, irregularly dispersed over the surface of the ovum, or exhibiting evidence of degeneration as shown by mucoid, hyaline and fibrous changes. Atrophy and hypertrophy of villi occur quite independently of any evidence of syphilis.

One useful result of this discussion would be a more careful investigation of the products of conception in abortions. Our present knowledge has accrued mainly from the work of anatomists, embryologists and, perhaps, experimental teratologists.

The question naturally arises as to whether these abnormal ova, so commonly aborted, are the result of inherent pathological attributes in the germ cells, or are caused by external influences. Some embryologists consider that pathological forms are caused by external influences and not by defects in the ovum or spermatozoon. Factors associated with the immediate environment and nutrition of the developing ovum appear to be the deciding points. One important argument in support of the influence of environment is the fact that when the ovum is implanted in an abnormal position, e.g., in the Fallopian tube, 96% of the embryos are abnormal (Ref. Mall, from investigation of forty-six specimens of tubal gestation in Kelly's clinic). Another important argument is that every form of abnormal embryo and monster—including spina bifida and anencephalus—known to occur in man, can be produced by artificial means from normal ova and embryos. Morgan discovered that spina bifida can be produced by subjecting frog eggs to the action of common salt. With a 0·7% solution, 100% of this abnormality can be obtained. Stockard, by the use of magnesium solutions, produced cyclopia in 50% of fishes. Herbert and Morgan found that when sea-urchin and frog eggs are submitted to the action of lithium salts, inversion of the blastodermic membranes occurs, leading to the production of nodular atrophic embryos. Loeb, experimenting with calcium salts, says that the action of calcium is specific in retarding the growth of the heart and blood-vessels, and indirectly the development of the embryo in general. Pathological embryos, if they survive, produce monsters, and it is perhaps a satisfactory provision of nature that so many of these abnormal ova die and are aborted. The factors which produce the abnormality usually exert such a radical influence that the lesions produced are

incompatible with further development. The ovum then becomes a foreign body, and in due course is expelled by the uterus. Fortunately, only a very small number of pathological ova develop to term, and inasmuch as such a large proportion of aborted ova are pathological, the question has been raised as to whether it is justifiable to attempt to prolong a pregnancy when abortion is threatened before the process of placentation of the ovum is completed. I can recall two instances in which abortion was averted only to result in the subsequent birth of children with anencephalus and spina bifida respectively.

*Nutrition of the Ovum.*—It is evident, then, that impairment of nutrition, the result of faulty implantation, abnormal food factors, or toxins such as may be present in the maternal blood or in a pathological decidua, is a potent factor in the causation of early abortion. The maintenance of an adequate source of food materials is effected in a different manner in different members of the mammalian family. In the case of certain ungulates the secretion of the uterine glands, known as uterine milk, an albuminous fluid containing cast-off cellular elements, is the only source from which the developing embryo and fœtus obtain nutriment. In others it appears to form an equal source with the direct exchange between the fœtal and maternal blood. In some sections of early human ova, there is evidence of destruction, by syncytium, of the dilated glands in the decidua, therefore it is possible that the high calcium and iodine content of the uterine secretion might have some bearing upon the nutrition of the early embryo during the stage of syncytial proliferation. On this point Professor Arthur Robinson wrote to me as follows:—

"In the case of the human subject it seems very probable that the secretion of the uterine glands plays no part in the nutrition of the embryo. It is true that in some cases the glands are opened up by the syncytium and blood is effused into the glands, but in such cases the gland epithelium does not appear to be actively secreting; and it is very likely that the blood effusion is accidental. During its passage through the Fallopian tube the zygote does not grow, it merely divides and becomes a mass of cells. It is not known how long the human zygote lies in the uterine cavity before it enters the mucosa, but the time must be short. Therefore, the time for nutrition by uterine contents must be brief. The time the human zygote depends upon destroyed mucosa must also be short, for the enclosure of dilated maternal capillaries and the destruction of their wall take place very soon. Therefore the human zygote is dependent upon absorption from the maternal blood except for a very short time."

This reasoned opinion appears to dispose of the possibility of the nutritive value of the uterine secretion in the human uterus, except for a very short period in the life of the ovum, unless there is some absorption or diffusion of the secretion to the surrounding decidual cells from the large dilated glands in the "stratum spongiosum." There appears to be little doubt, however, of the importance both of calcium and iodine to the developing ovum. The value of iodine is being appreciated more and more by stock-raisers throughout the world. An experiment at the Staffordshire Farm Institute showed that sows receiving iodine farrowed 50 per cent. more young than sows that had no iodine. At the Royal Experimental Station, Budapest, when iodine was given to pregnant sows, the average weight of the farrows at weaning was nearly 50 per cent. over that of the group that received no iodine. In the case of birds, the Rowett Institute and West of Scotland Agricultural College found that the egg yield from pullets receiving iodine went up 50 per cent. in one year over that from hens which had received no iodine in the diet. Indeed, the aggregate egg production when iodine was given in the form of potassium iodide was nearly double that of a pen where iodine was withheld. The subject of the transmission of various food factors and chemical substances from the maternal blood to the developing embryo for its essential development, has perhaps not received the attention it deserves at the hands of obstetricians. It is here that Comparative Medicine may afford very real help. We know that certain toxic agents, e.g. lead, which are transmitted act deleteriously upon the development and function of the

syncytium. We know very little, however, about organic toxins which may develop in the maternal organism, and which act in a similar manner. Still less do we know about the food factors which are essential for healthy embryonic development. In this connection the anti-sterility vitamin, fat-soluble E, is deserving of very serious consideration. In 1922, Evans and Scott published the first of a series of papers upon the "existence of a hitherto unknown dietary factor essential for reproduction." This specific vitamin has been the subject of detailed study in the Californian laboratories since that date, and in 1927 Evans and Burr published the results of their collective observations in an elaborate monograph. If their observations are confirmed the work of Evans and his collaborators is of far-reaching importance. It opens up indeed a new and fertile field of inquiry into the possible causes of some obscure early abortions and cases of sterility in the human subject. Working with rats, Evans found that although fertilization and implantation of the zygote occur in the absence of vitamin E, the embryos begin to die on the eighth day, and are later absorbed, together with the placenta. These embryos from animals fed on an E-free diet show general under-development most marked in the mesoderm. In the yolk sac there is a reduction in the size and number of the entodermal villi and also of the mesodermal blood islands. At a later stage there is impairment in the outgrowth and differentiation of the allantois. The distribution of the vitamin appears to be greatest in certain leaves and seeds, especially lettuce, wheat-germ, peas, alfalfa, bryophyllum and begonia, &c. The potency of these substances, especially lettuce and alfalfa, is apparently not lost by drying and desiccation at a temperature of 100° C. The value of wheat is due exclusively to the storing of vitamin E in the germ, as white flour is powerless to produce a cure in animals rendered sterile by feeding on vitamin E-free rations. A considerable amount of detailed work on the purification of vitamin E has been carried out by Evans and Burr, and its relation in composition and physical properties to vitamin A, cholesterol and biosterin is shown in Table VII.

There is one other aspect of this work to which I draw special attention and that is the resemblance in certain physical and chemical reactions which vitamin E presents to the particular ovarian hormone investigated by Doisy, Allen, Dickins, Dodds, Wright and others. "The partial destruction during vacuum distillation at 200° C., the total destruction by acetyl chloride and bromine, the stability to hydrogenation in the presence of platinum black, the molecular weight and elementary analysis all show a general similarity of the ovarian hormone to vitamin E." There is, however, marked contrast in the solubility of the two substances. The relation which the ovarian hormone has to decidual development, and growth of the embryo, is therefore, a matter of considerable interest. Indeed, it appears not improbable that this same biochemical growth factor present in the ovarian secretion may account for the rapidity of growth and the size of certain ovarian neoplasms of a metastatic nature. Time alone will prove the practical value of vitamin E and other food factors in the prevention of abortion and cure of sterility in the human subject. It is difficult, of course, in any isolated case to know whether a given result is *post* and not *propter* treatment.

In conclusion, I will quote brief clinical details of two cases in which the exhibition of antenatal therapy on these lines appeared to have a beneficial effect.

*Case I.*—Mrs. L., aged 40, married for three years. Her first pregnancy terminated at the seventh month with the stillbirth of twins. The next gestation aborted at the twelfth week. The third pregnancy again ended with the birth of a macerated fœtus at about the twenty-eighth week. The Wassermann reaction in the case of both husband and wife was negative and no obvious cause could be found to account for the obstetric clinical history. In March, 1926, the patient again became pregnant and she was immediately placed upon a diet rich in vitamin E, together with calcium lactate (gr. 60 per diem) and a preparation of ovarian hormone. The pregnancy progressed to term in a normal manner and a child weighing 10½ lb. was delivered by Cæsarean section, December 22, 1927.

*Case II.*—Mrs. S., aged 32, a 2-para. Her first child was premature, weighed 6¼ lb., and was reared with difficulty. The second pregnancy was complicated by hydramnios, and a child showing an extreme degree of spina bifida was born at the thirty-second week of gestation. The patient became pregnant again at the end of November, 1928. She was placed upon a similar régime and a healthy child weighing 8 lb. was born in September, 1929. The existence of a small elongated dimple over the lower part of the lumbar spine and sacrum showed the tendency to spina bifida which had complicated the preceding gestation.

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TABLE I.—SHOWING INCIDENCE OF ABORTION AMONGST PATIENTS ATTENDING GYNÆCOLOGICAL CLINIC (GENERAL HOSPITAL, BIRMINGHAM).

| | Cases | Total pregnancies | Abortions | Per cent. of abortions | Ratio of abortion to pregnancy at term | Patients who aborted | Patients who did not abort | Per cent. of women who aborted |
|---|---|---|---|---|---|---|---|---|
| *Pre-War* | | | | | | | | |
| 1909-1913 | 1,208 | 6,021 | 1,067 | 17·7 | 1 : 4·6 | 511 | 697 | 42·3 |
| *Post-War* | | | | | | | | |
| 1924-1928 | 1,148 | 3,910 | 663 | 16·9 | 1 : 4·8 | 397 | 751 | 34·5 |
| *Private* | 653 | 1,499 | 242 | 16·1 | 1 : 5·1 | 156 | 497 | 23·8 |
| Total | | | | | | | | |
| 1909-1928 | 3,009 | 11,430 | 1,972 | 17·2 | 1 : 4·7 | 1,064 | 1,945 | 35·3 |

TABLE II.—SHOWING RELATION OF ABORTION TO PARITY.*

| | Sterile | Abortions | | | | | | | | | Total Abortions | Total cases |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | *1* | *2* | *3* | *4* | *5* | *6* | *7* | *8* | *9* | | |
| 0-para | 265 | 47 | 14 | 5 | 3 | 2 | — | — | — | — | 71 | 336 |
| 1-para | — | 45 | 7 | 7 | 1 | 2 | 2 | — | — | — | 64 | 153 |
| 2-para | — | 49 | 6 | 3 | 2 | — | 1 | — | — | — | 61 | 221 |
| 3-para | — | 39 | 16 | 6 | 1 | 2 | 1 | — | — | — | 65 | 176 |
| 4-para | — | 31 | 5 | 4 | — | — | 1 | — | — | — | 41 | 122 |
| 5-para | — | 15 | 5 | 7 | 1 | — | 1 | — | — | 1 | 30 | 72 |
| 6-para | — | 8 | 4 | 2 | — | — | 1 | — | — | — | 15 | 42 |
| 7-para | — | 11 | 3 | 2 | 1 | — | — | — | — | — | 17 | 30 |
| 8-para | — | 6 | 2 | 2 | 2 | — | — | — | — | — | 12 | 24 |
| 9-para | — | 4 | 1 | 2 | — | 2 | 1 | — | — | — | 10 | 18 |
| 10-para | — | — | 1 | 1 | — | — | — | — | — | — | 2 | 8 |
| 11-para | — | — | 1 | 2 | 1 | 1 | — | — | — | — | 5 | 9 |
| 12-para | — | 5 | 2 | 1 | — | — | — | — | — | 1 | 9 | 15 |
| 13-para | — | 1 | 2 | — | 1 | 1 | — | — | — | — | 5 | 5 |
| 14-para | — | — | 1 | — | — | — | — | — | — | — | 1 | 2 |
| Total | 265 | 261 | 70 | 44 | 13 | 10 | 8 | — | — | 2 | 408 | 1233 |

* In this table the figures refer to *individuals*. For example, 45 primiparæ had 1 abortion, 7 had 2 abortions, etc.

TABLE III.—SHOWING PERCENTAGE OF INDIVIDUALS WHO ABORT IN RELATION TO PARITY.

(*Based on numbers in Table II.*)

| Sterile | 1-para | 2-para | 3-para | 4-para | 5-para | 6-para | 7-para and over |
|---|---|---|---|---|---|---|---|
| 21·1% | 41% | 27·6% | 36·9% | 33·6% | 41·6% | 35·7% | 54·9% |

TABLE IV.—SHOWING DISEASES ASSOCIATED WITH ABORTION.

| | | | |
|---|---|---|---|
| *Cases investigated* ... ... ... ... ... ... ... | | | 300 |
| *Diseases of Uterus* | | | |
| Neoplasms ... ... | Fibroids ... ... ... | | 21 |
| | Adenomatous polypi ... | | 4 |
| | Carcinoma cervicis ... .. | | 32 |
| | ,, corporis ... ... | | 3 |
| Displacements ... | Prolapse ... ... ... | | 30 |
| | Retroversion ... ... | | 14 |
| | Anteflexion ... ... ... | | 1 |
| Inflammation ... | Metritis ... ... ... | | 23 |
| | Endometritis ... ... | | 14 |
| | Cervicitis ... ... ... | | 1 |
| Developmental ... | Hypertrophy of cervix ... | | 3 |
| | Cochleate ... ... ... | | 1 |
| Trauma ... ... | Ectropion ... ... ... | | 10 |
| | Fixation ... ... ... | | 2 |
| | Amputation of cervix ... | | 1 |
| *Diseases of Fallopian Tubes* | | | |
| Salpingitis (including pyosalpynx) ... ... ... | | | 29 |
| *Diseases of Ovaries* | | | |
| Neoplasms ... ... | Cystomata ... ... ... | | 5 |
| | Carcinoma ... ... ... | | 1 |
| | Ovariotomy ... ... | | 1 |
| Displacements ... | Prolapse ... ... ... | | 1 |
| Inflammatory .. | Fibrosis ... ... ... | | 1 |
| *Diseases of Vulva* | | | |
| Inflammation ... | Urethral caruncle ... ... | | 1 |
| | Chronic vulvitis ... ... | | 1 |
| | Gonorrhœal vulvitis ... | | 3 |
| | Bartholin cyst ... ... | | 1 |
| *Diseases of other organs* | | | |
| Pelvic peritoneum ... | Pelvic abscess ... ... | | 1 |
| | Pelvic adhesions ... .. | | 2 |
| | Endometrioma ... ... | | 1 |
| Appendix ... ... | Appendicitis ... ... | | 1 |
| Bladder ... . . | Cystitis ... ... ... | | 1 |
| Kidneys ... ... | Nephritis ... ... ... | | 2 |
| *Constitutional* | | | |
| Syphilis ... ... ... ... ... ... | | | 1 |
| Tuberculosis ... ... ... ... ... | | | 2 |
| Influenza ... ... ... ... ... | | | 1 |
| Thrombocytopænia ... ... ... ... ... | | | 1 (5 abortion) |
| Toxæmia ... ... ... ... ... | | | 9 |
| Debility following confinement ... ... .. | | | 2 |
| Menstrual epilepsy ... ... ... ... ... | | | 1 |
| *Abortions induced* | | | |
| Criminal ... ... ... ... ... ... | | | 6 |
| For tuberculosis ... ... ... ... ... | | | 1 |
| For cardiac disease ... ... ... ... ... | | | 1 |
| For toxæmia ... ... ... ... ... | | | 1 |
| *Abortion—cause unknown* ... ... ... ... ... | | | 58 (19·3%) |
| Abortion due to mental shock ... ... ... | | | 3 |
| Abortion associated with premature menopause ... | | | 1 |

(Evidence of chronic inflammation in pelvis either in relation with genital tract or pelvic peritoneum in 26·6 % of cases.)

TABLE V.—TOTAL NUMBER OF NORMAL AND PATHOLOGICAL OVA OF THE FIRST TWO MONTHS.

| | No. of normal | No. of pathological | Percentage of pathological |
|---|---|---|---|
| His's collection from all sources ... ... ... ... | 62 ... | 18 ... | 22 |
| His's collection, only the specimens obtained from midwives | 19 ... | 12 ... | 40 |
| Mall's collection first series (Nos. 1 to 126) ... ... ... | 61 ... | 28 ... | 32 |
| Mall's collection second series (Nos. 127 to 208) ... ... | 24 .. | 37 ... | 61 |
| Mall's collection third series (Nos. 209 to 379) ... ... | 52 .. | 65 ... | 56 |
| Mall's collection whole number (Nos. 1 to 404) ... ... | 151 ... | 138 ... | 48 |

TABLE VI.—CONDITIONS OF THE CHORION (MALL).

| | Number | Per cent. | Normal | Pathological | No record |
|---|---|---|---|---|---|
| (1) Vesicular forms | 19 | 12 | 6 | 11 | 2 |
| (2) Ova with neither amnion nor embryo | 29 | 18 | 6 | 22 | 1 |
| (3) Ova with amnion but without embryo | 15 | 10 | 3 | 11 | 1 |
| (4) Embryos of the 4th week | 4 | 3 | 0 | 3 | 1 |
| Embryos of the 5th week | 18 | 11 | 1 | 11 | 6 |
| Embryos of the 5½ week | 21 | 13 | 0 | 15 | 6 |
| Embryos of the 6th week | 13 | 8 | 0 | 10 | 3 |
| Embryos of the 7th week | 27 | 17 | 1 | 23 | 3 |
| Embryos of the 8th week | 10 | 6 | 2 | 4 | 4 |
| Embryos of the 9th week | 2 | 1·4 | 0 | 2 | 0 |
| Embryos of the 10th week | 1 | 0·6 | 0 | 1 | 0 |
| Total | 159 | 100·0 | 19 | 113 | 27 |

TABLE VII.

| Substance | Analysis C. | Analysis H. | Molecular weight | Possible formula | Iodine number | Acetyl number | Refractive index | Distilling temperature (degrees C.) |
|---|---|---|---|---|---|---|---|---|
| Cholesterol | 83·4 | 11·9 | 386 | $C_{27}H_{46}O$ | 65·8 | 131 | — | about 200 |
| Biosterin (Takahashi) | 81·0 | 11·0 | 402 | $C_{27}H_{46}O_2$ | 180 | 139 | 1·52517 (20) | 147 (0·02 mm.) |
| Vitamin A. fraction (Drummond) | 77·7 | 11·8 | 300 | $C_{20}H_{36}O_2$ | 124 | 215 | 1·4705 (20) | 180—220 (1—2 mm.) |
| Vitamin E. fraction (Evans and Burr) | 81·7 | 12·2 | 400 | $C_{36}H_{64}O_2$ | 220 | — | 1·5009 (20) | 200—233 (0·5 mm.) |

**Mr. O. Stinson:** Contagious abortion is one of the most important bovine diseases. The causal organism is the bacillus of Bang. The mode of infection is ingestion. The affected cows abort early or late. Generally speaking, the earlier the abortion, the less is the likelihood that sterility will follow. Many cows "go to term," but are sterile afterwards. Certain families are almost completely wiped out, whereas other families, going through the same wave of infection, suffer much less. Some remain carriers for the rest of their lives. Retention of the placenta is of frequent occurrence.

Sterility is a common sequel—temporary or permanent—and is the most important association of the trouble, which may be uterine, ovarian, or Fallopian tube infection. Ovarian cysts are common, as also is a persistent corpus luteum, the result of endometritis. The cysts are manually dispersed per rectum and per vaginam, and the same method, together with local uterine treatment, is used for expelling the corpus luteum. The dispersal of the latter is accomplished by treatment of the uterus alone, which proves that the condition is primarily uterine. Cystic ovary is commonly a cause of persistent œstrum. The above treatment is usually successful and the cows conceive.

*Inhibition of Œstrum.*—In some districts "œstrum" is only observed during two or three months in the year. The months associated with the natural process are usually July and August—when the cattle are getting natural food under natural conditions. In the winter they are mostly tied up indoors for about six months. Poor food also may bring about the trouble, and so may "high" feeding for milk production in some cows. The condition as seen in particular districts is frequently associated with a deficiency of iodine or calcium in the food. It is noticed mostly in cold districts. Want of exercise probably plays a part.

*Food Causing Genital Diseases.*—Certain indigestible foods, including musty and dusty hay, harvested during wet summers, causes abortion, torsion of uterus, retained placenta (the subject may not have aborted) and eversion of the uterus. These conditions predispose to sterility.

*Sterility associated with Acute Calcium Deficiency.*—Frequently when a cow is mated and the following day she suffers from the condition known as "milk fever"—a disease which occasionally follows "œstrum," and characterized by a low serum calcium content (from 3 to 6 mgm.%)—she does not conceive, though she may never have failed to conceive before. These cows are generally very good milkers.

*Non-œstrum associated with Hypoglycæmia.*—I have recently been investigating the disease in cows which has been hitherto known as post-parturient dyspepsia. I have ventured to call it bovine hypoglycæmic ketosis. Œstrum is not present in the subject of the disease, and its appearance frequently is one of the first signs of recovery. The milk yield is mostly out of all proportion to the severity of the constitutional symptoms.

*Causes.*—Lactation (in ninety-nine per cent. of the cases); high feeding for milk production; standing in hot byres throughout the winter.

The last but most important is sudden change to very cold weather. The disease is rarely seen in the south.

Various conditions of metabolic and endocrine upsets are frequent causes of early abortion and sterility. The pancreas appears to play its part single handed so far as economizing the sugar of the system is concerned; on the other hand, the suprarenals, pituitary, thyroids (and "œstrin") are fighting for more blood-sugar. In addition to hypo- and hyper-conditions of the last three glandular secretions, is there not a hyper-insulinic condition?

We know that abortion is associated with diabetes mellitus. A natural, but extra, secretion of pituitrin is supposed to bring about natural parturition.

*Production Experiments on Fowls.*—Diseased (deficiency) fowls (one or both sexes) are frequently associated with chickens dying in the shells.

Fowls can be prevented from laying (although previously prolific layers) by a change from a suitable "laying diet" to a fattening one. The shells of the eggs are frequently soft before the hens actually stop laying.

Fowls during the laying season, when suddenly experiencing cold weather, frequently lay eggs which are non-fertile. There may be in their case also a hypoglycæmia, as in the case of the cow.

Imperfectly formed eggs may be found in the abdominal cavity, or in the oviduct (due to obstruction). In the latter circumstance the hens develop the male comb and voice, become fat and are useless for laying purposes.

**Captain Stewart R. Douglas**: Apparently the most important causes of abortion in animals are bacillary infection, amongst others the abortion bacillus of Bang in cattle, and one of the Salmonella group in horses. Such infections are not generally recognized as a cause of abortion in the human species, but Professor Madsen, of Copenhagen, has informed me that amongst numerous cases of undulant fever occurring in Denmark, eight occurred in pregnant women, and that no fewer than seven of these women aborted. It might therefore be worth while for the gynæcologists and bacteriologists to coöperate in ascertaining if any bacteria were present in the uterus at the time of the abortion.

**Dr. Leslie Sheather** supported the last speaker's suggestion concerning a bacteriological search for a cause of abortion in the human subject. Investigation in this and other countries had shown that, of animals infected with the abortion bacillus, about 30% passed the abortion bacillus out in the milk supply. The bacillus could only do its work in animals which were sexually mature. Young animals could not be permanently infected with the abortion bacillus; if they could, it would probably mean the end of contagious abortion in this country, because of the immunity which would be conferred before the animal became sexually

mature. A number of workers had found that if calves were fed on the milk of cows which had the abortion bacillus, a positive agglutination test could be obtained with the serum of the calf, but for a few weeks only. The calf might still be fed on that milk, but the agglutination titre of the serum would gradually drop. That fact might serve as a guide in human practice. He did not know whether the blood of children born prematurely could be tested for any agglutination capacity.

**Dr. H. S. Forsdike** asked the veterinarians whether a persistent corpus luteum in the cow was responsible for sterility, and whether, on expressing the corpus luteum by squeezing the ovary through the rectum, the cow became pregnant at the next service.

**Mr. Leslie Pugh,** in answer to the last speaker, said that it was quite a simple matter to extrude the corpus luteum from the ovary of a cow by rectal manipulation. The corpus luteum persisted in some cases of sterility when there were any uterine contents, e.g., pus or a desiccating fœtus, and removal of this body would usually ensure the elimination of the pus or fœtus about the fourth day, with a return of œstrum. In the case of the desiccated fœtus, the female almost invariably conceived at the next service.

The foundation of many cases of sterility was laid at the termination of the previous pregnancy. Both bitches and cows were not infrequently infected *in utero* several days before parturition, so that metritis was sure to occur whether they were handled by man or left alone. This suggested the possibility that some cases of puerperal fever in women might take their origin previously to an apparently normal confinement and that the attending surgeon or nurse might be wrongly blamed for transmitting the infection.

**Dr. A. E. Giles** (Chairman) said gynæcologists had almost come to the end of their present knowledge on both sterility and abortion, and that what the veterinarians had said in this discussion suggested that there might be in women a specific infection comparable to that seen in certain animals. Further, Dr. Sheather's observation that the Bang bacillus was found in the milk, had led to the idea in his (the speaker's) mind that if the milk of a woman who had aborted could be carefully examined, some light might be thrown on the subject.

He felt somewhat confused as to the points of view advanced by Professor Robinson and Professor Whitehouse. Professor Robinson appeared to think that the pathological ova were due, in a measure, to conditions inherent in the germ cells and not exclusively to environmental defects. Professor Whitehouse, on the other hand, said that embryologists believed that pathological ova were the result of abnormal environment, and were not due to any inherent factor in the germ-cells. He (the Chairman) would like to have his doubts resolved on that point.

**Professor Robinson,** in reply, said that most of the abnormalities were not due to environment but were inherent, though he granted that their bad environment had also its influence.

Care was needed in comparing cattle with human beings. In cattle, the nutrition depended largely on the uterine glands, and anything which interfered with that nutrition had a bad effect with regard to the pregnancy. In human beings, nutrition did not depend on uterine glands to any practical extent.

As to micro-organisms, he had shown on the screen groups of dead ova which had no micro-organisms at all; indeed, if organisms had been a factor they would have infected all the ova. Apparently the conditions were the same in ova which died, and in those which did not die. In abortion the dead zygote was there, and must be got rid of in the quickest way, namely, by abortion and not by absorption.

Vitamin E was present in all diet, and it was present in ordinary flesh. If there was anything in the mother's tissues required by the fœtus, the fœtus would get it.

**Mr. Barker,** in reply, said it was a fact that in some cases the expressing of the corpus luteum would produce œstrum in three or four days, and service thereafter would result in a perfect pregnancy, but in a number of cases this was not the sequence. He thought that the œstral hormone had some effect on the corpus luteum of the previous œstrum. In cattle the corpus luteum at the eighteenth day was declining, and it might be that this decline was associated with some lysis.

**Professor Whitehouse** (in reply) said that he was in the unfortunate position of apparently disagreeing with his old teacher, Professor Robinson. Professor Robinson had pointed out that abnormal embryos, in the case of ferrets, occurred in what appeared to be normal and healthy uteri, and therefore he argued that the defect must lie in the germ cells. There was, however, the equally important fact that in the absence of a well-developed decidua, such as in tubal gestation, not 1%, but 96% of the embryos were abnormal. The decidual organ was all-important in the nutrition of the embryo, and the problem was as intimately concerned with physiological function as with anatomical structure. Even if the uterus of a ferret appeared to be the same at all points, was it correct to argue that the physiological nutritional power was also the same? The site of implantation of the ovum in the uterus might be a very important factor in the establishment of an abnormal environment. The issue was very debatable and the truth probably lay between the two divergent views. Possibly both were correct on occasion. As to the question of vitamin E and its presence in the bodies of rats, Evans had referred to this point in his monograph. The flesh of every rat, or for that matter every other animal, only contained such vitamin as had been introduced at birth, or added subsequently by feeding. It was possible, by suitable rations, to exhaust that supply. When a rat had been rendered sterile by withholding vitamin E from its diet, it was not possible to render it fertile by simply feeding it upon the flesh of any rat; it must be fed by the flesh of such an animal as already contained an adequate supply of the essential factor.

Referring to infection with the Bang bacillus, he had met with one instance in 1916, that of a woman living on a farm in Worcestershire, where the *Bacillus abortus* was operative. The bacillus had been isolated directly from the uterine discharge. The woman had fever at the time. After that case he had taken cultures from the next fifty abortions he encountered, but he had never found the Bang bacillus again, and he regarded it as a rare cause of abortion in the human species.